A STUDY OF THE EFFECTS OF THIAMINE ON CHILDREN WITH SPEECH NON-FLUENCY

by
EDWARD M. PENSON

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CHAPTER I

INTRODUCTION

The objective of this chapter is to describe the background of research, reporting, and reasoning by authors of relevant literature which points to the rationale of the present study and makes clear its purpose.

Statement of Purpose

It is the purpose of the present work to study the effects of thiamine (vitamin B_1) upon children whose speech has been rated by trained judges as "non-fluent."

Review of Stuttering Theories and Research

For over two thousand years the problem of stuttering has been a subject of study, theorization, and treatment.[1] During this time, people who have stuttered have been exposed to varying kinds and degrees of superstition and quackery, scientific research, and rational treatment. Even so, the origin of stuttering remains, to a large extent, unknown. This does not appear to be due to a lack of effort expended or time consumed on the subject. There have been many varied

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[1] G. M. Klingbell, "The Historical Background of the Modern Speech Clinic," The Journal of Speech and Hearing Disorders, IV, Part I (June, 1939), 115.

descriptions of symptoms, theories of causation, and attempts at treatment. The following historical background on the subject of stuttering is not meant to be all-inclusive, but it should serve to illustrate the long and varied history of stuttering as a problem for study.

In its early history, according to Bryngelson, stuttering was thought to be caused by gods and devils and therefore related to the soul of man.[2]

Klingbell recorded that Herodotus, the Greek historian, (c 484 - 424 B.C.), reported the treatment of Battos, son of Polymnestos, by a Pythian priestess. She recommended emigration south to Libya so that he might escape the evil god causing his affliction.[3]

Later, the tongue became the center of attention as is suggested by the many theories ascribed to it and the many treatments prescribed for it. According to Klingbell's historical account, Aristotle (c 384 - 322 B.C.) was among the first to describe the cause of stuttering as being centered in the tongue. Aurelius Celsus (c 42 B.C. - 37 A.D.), an early medical encyclopedist, agreed with Aristotle and suggested a treatment regimen which included massaging the tongue and throat, eating pungent substances, and performing physical and respiratory exercises. Galen, (c 131 - 201 A.D.) recommended cauterization of the tongue. In the sixth century Petius believed a cure for

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[2]Bryng Bryngelson, "Investigations in the Etiology and Nature of Dysphemia and its Symptom, Stuttering," The Journal of Speech Disorders, VII (March, 1942), 15.

[3]Klingbell, "The Historical Background of the Modern Speech Clinic," op. cit., 115.

stuttering could best be accomplished by a division of the frenum. An Arabian king's court philosopher and physician, Abu Ali Al Husain Avicenna, (980 - 1037) blamed stuttering on the tongue, lesions of the brain and nerves, accompanied by spasms of the epiglottis. Frances Lord Bacon appears to have been of the opinion that stuttering and other speech defects are caused by the coldness and dampness of the tongue, or — on occasion — by its dryness. If the tongue were hot and dry, he suggested ice or cooled lotions be applied. If the tongue were too cold or damp, he prescribed internal applications of wine. Klingbell pointed out that some of the early alleged authorities traced the cause of stuttering from the tongue to other structures. For example, Johann Gottfried von Hahn, court physician to King Frederick, blamed all speech defects on the hyoid bone.

In his discussion of stuttering etiology, Bryngelson indicated that Galen and Petius were among several of the early experts who attempted surgery on the tongue in an effort to cure stuttering.[4] By and large, this surgery apparently had as its objective the elevation of the tongue. Some surgeons cut a transverse wedge into the tongue and sewed the edges of the gap together. Bryngelson reported that stuttering symptoms frequently disappeared following surgery because loss of blood, surgical shock, or infection had caused the patient's death. Other attempts at a surgical cure for stuttering consisted of the removal of the tonsils and uvula. Gertz employed peppermint oil

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[4]Bryngelson, "Investigations in the Etiology and Nature of Dysphemia and Its Symptom, Stuttering," op. cit., 16.

and chloroform in an effort to allay the spasms of the stutterer's diaphragm.

The emergence of physiologic theories was advanced by the belief that stuttering represented an asynergy — a malfunctioning of the musculature involved in speaking. The therapy consisted of phonetic drills to induce better coordination. Darwin appeared to be the founder of this school of thought, and among its other exponents Bryngelson listed Carpenter, Hunt, Kussmal, Gutzman, Wyllie and Bell.

Makuen, Kenyon, Kyle and Martin represented a point of view which considered stuttering to be a physical habit due to a disoriented psyche.[5] The treatment suggested in this instance was still largely physical, but the transition to a theory expounding psychological treatment, as well as causation, was rapidly forthcoming. Bryngelson made careful note of this change:

> Now stuttering was interpreted as being the result of a basic emotional instability — a 'complex,' social morbidity, or hyperactivity of the affective life of the stutterer. Even modern medical books mentioning stuttering, describe it in this fashion. Although the questionaire method was used at first, better results were proclaimed when the doctor and patient could work clinically in conference. Mental hygiene and psychotherapy were the vogue in treatment. Fletcher and Bluemel were the two most outstanding exponents of this school. In crept the ideas of Blanton and Swift. The former thought that stuttering was due to transient auditory amnesia; the latter — visual central asthenia. Images by these men were treated like specific organs had been treated at an earlier period.[6]

As psychoanalysis began to have its influence in the field of

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[5] Ibid.

[6] Ibid.

mental health, its effects were also felt in the field of speech therapy. Appelt, Rosenbach, Dubois, Coriat, Steckel, Netskatschen, and Hudson advocated psychoanalytic treatment for the "speech neuroses."[7]

Orton and Travis in the 1920's, introduced a modern scientific approach to the study of this seemingly mysterious phenomenon — stuttering. This approach included laboratory and clinical research which attempted to discover differences, physiological and/or psychological, between stutterers and non-stutterers. It would seem that if such differences could be found, they might provide important clues as to the nature of the cause or causes of stuttering.[8]

Robert West summarized the observable differences between stutterers and non-stutterers as follows:

> There are certain demonstrable differences between the stutterer and the non-stutterer, aside from the spasms that occur during speech. The chief of these are (1) the slowness of diadochocinesis of the stutterer's articulatory muscles and (2) his lack of vocal inflection.[9]

West went on to suggest that these two differences may be related; the lack of inflection being a manifestation of a spasticity of musculature, which also causes sluggish articulatory movements.

Emil Froeschels indicated that "Stuttering is a nervousness,

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[7]Klingbell, "The Historical Background of the Modern Speech Clinic," op. cit., 121.

[8]Bryngelson, "Investigations in the Etiology and Nature of Dysphemia and Its Sympton, Stuttering," op. cit., 16-17.

[9]Robert West, Lou Kennedy, and Anna Carr, The Rehabilitation of Speech (New York: Harper & Bros., 1947), 87.

which as a rule rises in early childhood."[10] James S. Greene, when describing the underlying characteristics of stuttering wrote, "Stuttering is a nervous affliction."[11] He further suggested that some children have an inherited nervous constitution predisposing them to stutter. He explained that they may go along without any difficulty unless a trauma or accident occurs to precipitate the disorder. He described the onset of stuttering in this way:

> Stuttering isn't simply a bad habit that time will cure — it is a nervous disorder. It is a signal that the child is meeting some situation, or is under some strain with which his nervous system cannot adequately cope.[12]

Lee Edward Travis seems to have had this point of view in mind when he wrote:

> The stutterer, as do most other types of speech defectives, represents a certain lack of maturation of the central nervous system which results either in malignation of the highest neurophysiological levels involved in speech or the predisposition of these levels to disintegration when exposed to nociceptive stimuli.[13]

According to Eugene F. Hahn's summarization, E. J. Boone, a British authority, appeared to concur with Travis. Boone considered the causes of stuttering to be two:

> The endogenous or constitutional, by which the child

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[10] Emil Froeschels, "Differences in the Symptomology of Stuttering in the U. S. and in Europe," The Journal of Speech Disorders, VI (March, 1941), 45.

[11] James S. Greene, "Hope for the Stutterer," Hygeia, XXIV (February, 1946), 120.

[12] Ibid.

[13] Lee Edward Travis, Speech Pathology (New York: D. Appleton & Co., 1931), 254.

> inherits neuropathic tendencies, which predispose him to stammer; the exogenous or environmental factors, among which are included shock, fright, illnesses, and strain. The instability of the nervous system is the primary cause of stammering, while the environmental factors, by weakening the individual's physical and psychical resistance, serve to reveal the latent tendency. The actual stammer is not inherited, but the child may inherit the nervous instability of the parents. The secondary factors will then contribute to the general instability of the nervous system.[14]

A psychosomatic theory of stuttering has been presented by I. W. Karlin. He related the development of myelinization to the onset of stuttering. He believed that the slower the development of myelinization, the greater the chance for stuttering. The stuttering is then enhanced by environmental pressures. He stated:

> If stuttering continues, emotional factors and habit formation begin to play a greater role in perpetuating this disorder. In the older child and in the adult the emotional factors and established neuromuscular habits become the predominant causative agents of stuttering.[15]

West, then, would seem to have found some justification for the many theories which suggest a relationship between stuttering and the nervous system. Using a neurological test for stutterers, he found that in slowness of diadochocinesis, stutterers resemble spastics. The stutterer's lack of vocal energy, according to West, suggests "a lack of muscular energy — an asthenia — an inability to produce inflections because inflections require muscle contractions and the energy is not available."[16]

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[14] Eugene F. Hahn, Stuttering: Significant Theories and Therapies (Stanford University Press, Stanford University, 1943), 122.

[15] I. W. Karlin, "A Psychosomatic Theory of Stuttering," The Journal of Speech Disorders, XII (September, 1947), 322.

[16] West, The Rehabilitation of Speech, op. cit., 87.

With West's findings in mind, it seems relevant to take note of an experiment which tested the effect of prostigmin on ten chronic stutterers. Prostigmin, a tension-reducing drug which acts to depress the muscle tone, was administered to stutterers from fourteen to forty years of age for fourteen months. The dosage was four 15 mg. tablets a day. For the duration of the experiment, speech training was intentionally avoided. The authors concluded:

> There seemed to be good reason to believe that prostigmin did have some effect on the severity of the spasm — during the early weeks of its use and possibly later, making it easier for patients to manage the stutter . . . the tension created by the severe spasms was reduced. . . . To all outward appearances the stutter is a muscle spasm.[17]

Although there seems to be some agreement as to the importance of the neuromuscular differences between the stutterer and the non-stutterer, the unanimity is neither complete nor enduring. This seems to be the point of departure at which place researchers embark in many different experimental directions. It would seem wise to consider, at this point, then, the possible underlying or less observable differences between the stutterer and the non-stutterer which might have causative or effective relation to the already mentioned observable difference of hypertonicity.

There have been numerous metabolic and biochemical studies made along this line, and an account of some of these studies should help lead the way toward seeing the justification of the present research

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[17] Howard J. Schaubel and Roy F. Street, "Prostigmin and the Chronic Stutterer," The Journal of Speech and Hearing Disorders, XIV (June, 1949), 143.

in a clear light.

In 1922, H. E. Starr gave the following reasons for selecting the saliva as a means of investigating the relationship metabolism might have with stuttering:

> This fluid is constantly being secreted, swallowed, and passed through the physiological cycle. It may be readily collected for examination at all times and places. It may be regarded practically as transformed protoplasm of the secreting cell, with admixture of salts and other substances virtually dialysed from the blood, and affected to a greater or lesser degree by the conditions obtaining in the oral cavity and by the constituents of the alveolar air. The glands of secretion have abundant neural connections with both the cranial and sympathetic nervous systems. Thus of the three principal sets of salivary glands -- sublingual, submaxillary, and parotid -- each one is innervated by both cranial and sympathetic nerves.[18]

The results of Starr's research showed that 73.7 per cent of the stammerers examined in his survey of the University of Pennsylvania Speech Clinic were sub-breathers, and had their systems overloaded with carbon dioxide.[19]

In another study in 1929, Starr found that stutterers have characteristic high alveolar carbon dioxide as opposed to non-stutterers. He stated:

> It is quite evident that the sub-breathing stammerer is overloaded with carbon dioxide. Not overloaded beyond physiological limits to such an extent to be classified as pathological, he is overloaded beyond the limits of the psychologically normal. As he improves under treatment,

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[18] H. E. Starr, "The Hydrogen Ion Concentration of the Mixed Saliva Considered as an Index of Fatigue and of Emotional Excitation, and Applied to a Study of the Metabolic Etiology of Stammering," The American Journal of Psychology, XXXIII (1922), 394.

[19] Ibid., 395.

> largely by means of intensive breathing exercises, his alveolar CO_2 diminishes and with it, of course, the partial pressure of the carbon dioxide in the blood.[20]

On the basis of his studies, Starr emphasized the relationship between psychological and physiological processes:

> We need simply to recognize the fact that the physiological parallels the psychological and is indicated by the chemistry of the individual . . . even motivation, that most psychical of psychological processes, is correlated with or parallels metabolism.[21]

E. B. Twitmyer reported a study made by M. Trumper which found a correlation between the types of breathing and the red cell count and hemoglobin content. This research included 101 subjects who showed symptoms of stuttering. Trumper concluded that shallow breathers have a hemato-respiratory compensation, which means that an increase in the red cell volume and hemoglobin content of the blood compensates partially for the inadequate respiratory reactions. He proposed that the scarcity of women stammerers is due, in part, to the lower viscosity of their blood, which in turn, is due to a lower red cell volume.[22]

James F. Bender commented upon the above findings of Trumper as follows:

> His finding of a high erythrocyte count in the stutterer's blood is especially important in the light of W. B. Cannon's researches that erythrocytes are increased during emotional changes and that the increase is due to a sympathetic

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[20] H. E. Starr, "Psychological Concomitants of High Alveolar Carbon Dioxide," The Psychological Clinic, XVII (March, 1928), 12.

[21] Ibid., 2.

[22] E. B. Twitmyer, "Stammering in Relation to Hemo-Respiratory Factors," The Quarterly Journal of Speech, XVI (June, 1930), 278-83.

> stimulation of the spleen. Thus, the high blood sugar content is believed to be indicative of the emotionality of the stutterer.[23]

Wendell Johnson, Genevieve Stearns, and Edna Warweg conducted a study in 1933 which had as its purpose the detection of any alterations in the chemical composition of the blood in stutterers which might show a relationship to the muscular spasms and increased muscle tonus in stuttering. They summarized the results of their research in this manner:

> 1. The serum calcium values of fifteen stutterers were found to be wholly normal, tending toward the upper limits of the normal range. These findings were interpreted as evidence that the increased muscle tonus and muscular spasms observed in stuttering are not associated with low calcium tetany in these cases.
>
> 2. No alteration in the normal relationships between serum calcium and serum potassium or inorganic phosphorus was observed.
>
> 3. The fasting blood sugar level of fifteen stutterers was not altered from the normal. Severe stuttering of one half hour's duration was insufficient to alter the level of blood sugar of one subject. It would appear, from these results, that the emotional reactions associated with stuttering in these cases are not associated with any disturbance of carbohydrate metabolism.[24]

George Kopp conducted metabolic studies of stutterers when he was at the University of Wisconsin. This research represented an effort to determine how the metabolism of the stutterer differed from that of the non-stutterer as evidenced by blood serum calcium,

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[23] James F. Bender, The Personality Structure of Stuttering (New York: Pitman, 1939), 33.

[24] Wendell Johnson, et. al., "Chemical Factors and the Stuttering Spasm," The Quarterly Journal of Speech, XIX (June, 1933), 413-14.

inorganic phosphate, potassium, chloride, cholesterol, non-protein nitrogen, albumin, total protein, globulin, and glucose. The reasons why Kopp chose the blood as the basis for his study would seem to lend further relevance to the present study.

> The blood is the medium in which all metabolic exchanges are made and is therefore the environment in which muscle and nerve tissue live and function. Since normal life and function are dependent upon a definite equilibrium of the blood contents, the converse holds that abnormal function may be due to a disturbed equilibrium of the blood contents as reflected in the metabolism and composition of the nerve and muscle. The composition of the nerve and muscle determines whether the reception of and reaction to stimuli of all kinds can be classified as normal. The nerve impulse is not an entity within itself. The clonic and tonic myospasms of the stutterer are factual evidence of abnormal function. It is evident that if the afferent, associational, or efferent nerve impulses of the stutterer differ, then somewhere along the nerve fiber, its cell or ganglion, will be found the change in composition that must predispose the change in the character of the impulse. Likewise if the musculature of the stutterer is different from that of the non-stutterer, the difference must be one of composition.[25]

The differences between the blood of the stutterers and the non-stutterers were mostly within the normal range. Kopp listed his findings as follows:

> Stutterers have a higher total serum calcium than non-stutterers.
>
> The inorganic phosphate is higher in stutterers than in normals.
>
> The potassium is lower in stutterers than in normals.
>
> The total protein, albumin, and globulin are lower in stutterers than in non-stutterers.
>
> There is no great difference in non-protein nitrogen

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[25] George Kopp, "Metabolic Studies of Stutterers," Speech Monographs, I (September, 1934), 123-24.

between the two groups.

> There is no appreciable difference in diffusible calcium, cholesterol, and chloride for the two groups.
>
> The stutterers have a high blood sugar as compared with non-stutterers.
>
> The blood pattern of the stutterer, as shown by the correlations of total serum calcium, potassium, inorganic phosphate, total protein, and non-protein nitrogen, is practically the reverse of the pattern of the non-stutterer.[26]

These findings led Kopp to conclude that, "Stuttering is a manifestation of a disturbed metabolism." Kopp believes that someday stuttering might be controlled by dietary means which would regulate the metabolism of the child. He added, "The metabolic changes which take place in producing and maintaining stuttering must first be established."[27]

In a study which compared the blood distribution among fifty stutterers and thirty-eight thousand people who had previously been typed in investigations carried on in the United States, Jeanette Anderson and Mary L. Whealdon found no significant differences in the blood distribution of stutterers and normals.[28]

I. W. Karlin and A. E. Sobel made a study of the chemical composition of the blood of twelve stutterers and twelve children with more normal speech. Each stutterer was matched with a non-stutterer of the

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[26] Ibid., 129.

[27] Ibid., 130.

[28] Jeanette Anderson and Mary L. Whealdon, "A Study of Blood Distribution Among Stutterers," The Journal of Speech Disorders, VI (March, 1941), 23.

same age, sex, height and weight. The authors found no statistically significant differences between the two groups.[29]

Because of his belief in the justification of nutritional studies of stutterers, Robert E. Card conducted research on the relationship of allergy to stuttering. He studied case histories of 104 stutterers and their families. He concluded that:

> Similarities between the factors of stuttering and asthmatic reactions; the positive histories of allergy in the stutterer's families; the fact that every stutterer tested showed a marked degree of sensitivity; and the degree of stuttering seemed to be in direct proportion to the severity of reaction to the intradermal tests — all of which indicates the likelihood of stuttering being in such cases a manifestation of allergic reaction.[30]

In 1938, A. M. Kennedy and D. A. Williams also found a relationship between stuttering and histories of allergy. In a study of one hundred stutterers, they found fifty-two stutterers had personal histories of allergy and, of the rest, all but one had family histories of allergy. They compared these one hundred stutterers with a group of one thousand non-stutterers of whom only 37 per cent had personal and/or family histories of allergy. On this basis, they concluded that some individuals have a predisposition to both stuttering and allergy.[31]

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[29] I. W. Karlin and A. E. Sobel, "A Comparative Study of the Blood Chemistry of Stutterers and Non-Stutterers," Speech Monographs, VII (1940), 82.

[30] Robert E. Card, "A Study of Allergy in Relation to Stuttering," The Journal of Speech Disorders, IV (September, 1939), 229.

[31] A. M. Kennedy and D. A. Williams, "Association of Stammering and Allergic Diathesis," British Medical Journal (December 24, 1938), 1306-1309.

E. M. Glaser, in 1936, conducted a survey of the possible relationship between stuttering and endocrine malfunctioning. The survey consisted of consulting twenty-nine endocrinologists concerning their experience with patients who stuttered. Among Glaser's findings is this report of Dr. Murray B. Gordon of the Long Island College of Medicine:

> . . . I reported five cases of childhood myxedema and hypothyroidism in children in which stammering occurred during the course of thyroid treatment. I considered it as a manifestation of a general nervous excitation following disturbance of the central nervous system. The stammering disappeared on discontinuing the thyroid extract and reappeared on its resumption.[32]

Dr. Harry A. Solomon, of Bellevue Hospital, wrote Glaser as follows:

> Two cases of stuttering occurred in a group of congenital thyroid insufficiency (cretin) cases. In no other form of endocrine dycrasia have I ever noted this defect. In adult hypothyroidism (myxedema), primary or secondary slowness of speech, jumbling and difficulty in pronouncing words is a constant feature. This is due to the disturbed function of the nervous system when deprived of the stimulating influence of a specific hormone, thyroxin.[33]

A more recent study concerning the relationship between endocrine malfunctioning and stuttering was reported by Marion Kramer in 1947. In an unpublished thesis, Kramer reported an experiment conducted at Stanford University Medical School in which it was found that epinephrine injections into women whose ovaries had been removed,

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[32] E. M. Glaser, "Possible Relationship Between Stuttering and Endocrine Malfunctioning," The Journal of Speech Disorders, I (September, 1936), 84.

[33] Ibid., 85.

caused difficulty in fluency resulting in temporary stuttering.[34]

Martin F. Palmer and Anna Mae Gillett conducted a study of twenty-one stutterers and twenty-four normal speakers. The study compared the heart rhythms of the two groups. The authors surmised that "Stuttering is the result of a sex-linked, neuro-physiologico-metabolic etiology."[35]

It becomes evident, in light of these related studies, that investigations concerning the possible neuro-physiologico-metabolic etiology of stuttering appear not only varied in their points of attack, but seem controversial in their conclusions as well. Cognizance must be taken of the frequency of inference and the temptation to theorize present in many studies of this nature. Harris Hill, in 1944, evaluated critically the biochemical investigations conducted up until that time:

> In all instances where differences between stutterers and normal speakers were purportedly obtained, the differences were compared with and shown to approximate closely, changes in so-called normal persons during muscular activity and effective behavior. . . . In case of biochemical differences, no findings warrant any assumption of special metabolic or chemical agents which are causal. The phenomena of stuttering can well be explained if principles of normal behavior are adhered to without attempting to make the stutterer a unique animal in the universe.[36]

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[34] Marion Kramer, "A Critical Examination of Studies on Physiological Aspects of Stuttering," (Unpublished M. A. thesis, Stanford University, 1946).

[35] Martin F. Palmer and Anna Mae Gillett, "Respiratory Cardiac Arrhythmia in Stuttering," The Journal of Speech Disorders, IV (June, 1939), 140.

[36] Harris Hill, "Stuttering; I. A Critical Review and Evaluation of Biochemical Investigations," The Journal of Speech Disorders, IX (September, 1944).

Granted, then, that there has been no conclusive evidence advanced which establishes physical, metabolic, or neurological differences between the stutterer and the non-stutterer which can be considered causal. However, it appears permissable, if not mandatory, that further study be undertaken in these areas. It should be clear that if evidence of such differences were to be uncovered, it would still be impossible to discount the research results which have accrued from developmental or environmental theories of stuttering causation. A brief review of the evidence supporting the environmentalist's point of view seems especially cogent here, because it will tend to demonstrate that the present study is not designed to refute this evidence, but rather the rationale of the current investigation is wholly consistent with and partly dependent upon the evidence already established by developmental or environmental research.

According to Wendell Johnson's diagnosogenic theory of stuttering causation, most children go through a period during which hesitations, repetitions and prolongations — non-fluency, per se, — are normal concomitants of speech utterance.[37] Johnson stated:

> These repetitions and hesitations are not accompanied by any apparent tension or anxiety on the part of the child. They seem to occur somewhat more frequently when the child is "talking over his head," when he lacks sufficient knowledge of what he is talking about, when the listener does not respond readily to what the child says, or his vocabulary does not contain the seemingly necessary words. Such conditions appear to occur often in the speaking experience of very

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[37] Wendell Johnson, People in Quandaries (New York: Harper & Bros., 1946), 445.

young children.[38]

Johnson further describes this non-fluency as occuring more frequently when the child is talking in the face of competition. More non-fluency seems to occur when the child has feelings of shame or guilt brought on by parental scolding or rejection. This is especially true when the scolding or rejection have reference to his right or ability to speak. There is also indication that non-fluency increases during "language spurts," such as during the transition from the use of single words to the speaking of short sentences, or from the utterance of simple sentences, or when the child begins to use the pronoun I in place of me.[39]

It is interesting to note that Johnson first became interested in studying the effect of labeling or diagnosing these non-fluent patterns as "stuttering," when he was made aware of the fact that among the Barnock and Shoshone Indians there are no stutterers. Upon investigation it was learned that these tribes had no word for "stuttering" in their language. They had a relatively permissive attitude toward speech and speech development, and, in fact, had no label to use, no name to call, and no differences to point-up regarding non-fluent speech.[40] It is this very act of labeling an otherwise normal pattern of speech that Johnson believes brings on the feelings of anxiety, tension, and fear of speaking situations so evident in the older stutterer. The fear leads to avoidance attempts, and these attempts, in turn,

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[38] Ibid.

[39] Ibid., 446.

[40] Ibid., 441.

result in hypertense, reinforced stuttering. It was Johnson's premise, then, that when a child is made to feel that his speech is thought of as different, wrong, abnormal, bad or stuttering, he will come to anticipate, apprehend, attempt to avoid the stuttering, and finally he will stutter with excessive tension.

Subsequent investigations by Johnson, those mentioned below, and others, have tended to support the cogency of Johnson's theory.[41] Some of the recent studies, for example, have established the vital influence of parents and their reaction to non-fluency.

Oliver Bloodstein investigated the possibility that parents of stutterers make diagnoses of stuttering more frequently than parents of non-stutterers. He found that parents of stutterers do diagnose stuttering more readily as "stuttering," and they also diagnose non-stuttering more quickly as stuttering.[42]

Using various scales of parental domination as tests for parents of stutterers and non-stutterers, John P. Moncur reported "Parental domination was indicated by the responses of more mothers of stutterers than by those of the mothers of the non-stutterers on all phases of the study."[43]

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[41] Wendell Johnson, et. al., "A Study of the Onset and Development of Stuttering," The Journal of Speech Disorders, VII (September, 1942), 251-57.

[42] Oliver Bloodstein, William Jaeger, and Jack Tureen, "A Study of the Diagnosis of Stuttering by Parents of Stutterers and Non-Stutterers," The Journal of Speech and Hearing Disorders, XVII (September, 1952), 308-09.

[43] John P. Moncur, "Parental Domination in Stuttering," The Journal of Speech and Hearing Disorders, VII (June, 1952), 155.

Although P. J. Glasner conducted a study which demonstrated that "No specific emotional or environmental factor produces stuttering with any significant regularity," he did find that environmental pressures, especially speech pressures, were foreground in the stuttering picture.[44]

Granting, then, that there does appear to be a vital relationship between environment and the ontogenesis of stuttering, we still cannot exclude from the realm of possibility that non-environmental differences do exist between individuals who are relatively susceptible to environmental pressures and those who are relatively unsusceptible. The search for neuro-physical or metabolic differences between adults has revealed nothing of significance. However, the extreme paucity of stuttering research dealing with children has left many investigative stones unturned. Charles Van Riper concurred with this belief when he stated, "Much of the mystery of stuttering is due to the tendency of investigators to confine their observation to the adult case, with little regard for the development of the disorder. The research on children has been meager. . . ."[45]

It has been previously stated that it was the purpose of the present work to study the effects of thiamine (vitamin B_1) upon children whose speech has been rated by trained judges as "non-fluent." Such a

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[44] P. J. Glasner, "Personality Characteristics and Emotional Problems in Stutterers Under the Age of Five," The Journal of Speech and Hearing Disorders, XIV (June, 1949), 138.

[45] Charles Van Riper, Speech Correction Principles and Methods, 3rd. ed. (New York: Prentice-Hall, Inc., 1954), 343.

study might or might not uncover physical differences between fluent and non-fluent children. The factor of differences was not the primary concern. The principle interest of such an investigation has been described by Elizabeth R. Alexander, who did the exploratory forerunner of the current project. She stated:

> It has been agreed that hesitant speech among children learning to talk is not only common, but quite normal and that pathological stuttering is instilled only when these tendencies become complicated by personality conflict. Emotional reactions on the part of the child to his non-fluency in turn may accelerate the development of his stuttering. Hypertensions, fatigue, restlessness, and general nervous irritability which appear so consistently among children who seem to have a predisposition to stutter, suggest that treatment to reduce these factors might have a secondary effect of reducing the tensions of the faltering speech.[46]

Having completed a review of stuttering theories and research, and having stated the purpose of the present work, it becomes necessary to explain the possible relationship of thiamine to speech, and specifically, to non-fluent speech. That which follows will include a description of thiamine, its biological function and therapeutic uses, its history and nutritional sources, its role in carbohydrate metabolism, and its relationship to the central nervous system.

Thiamine and Nerve Integrity

Several elementary, but necessary, definitions will aid in the exposition of thiamine and its relationship to the present study.

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[46] Elizabeth R. Alexander, "An Experimental Study of the Effectiveness of the Administration of Thiamine Hydrochloride in Preventing Stuttering Among Pre-School Children," (Unpublished M. A. thesis, University of Florida, 1950), vi.

1. Vitamin: According to Walter Eddy, a vitamin is a chemical compound whose presence in the diet is essential to the maintenance of growth and health, and whose absence from the diet or inadequate supply results in specific manifestations of ill health or pathology.[47]

2. Thiamine: The word "thiamine" will be the preferred symbol for that vitamin of the B-complex group occasionally called thiamine hydrochloride, vitamin B_1, or aneurine.

3. Cocarboxylase: Cocarboxylase is the active form of thiamine in tissue oxidation. It is the thiamine pyrophosphate (pyro — an acid formed from another acid by action of heat, and pyrophosphate — a salt of pyrophoric acid).

Eddy's brief historical account of thiamine, indicates that it was first isolated, in 1925, by Jansen and Donath. Later, Williams improved their yield and established the chemical nature of this vitamin.[48]

Eddy explains that "study of biological oxidation has shown that many of the vitamins are actively concerned in oxidation reactions. They form important action or 'prosthetic' groups in the enzymes and coenzymes that the body uses for transport of hydrogen, or activation of oxygen in the oxidations by which food energy is made available.[49] Since the principal fuel food is sugar, when sugar is oxidized in

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[47]Walter H. Eddy, What Are the Vitamins? (New York: Reinhold Publishing Corp., 1941).

[48]Ibid.

[49]Ibid.

tissue cells, it is converted into water and carbon dioxide, and energy is liberated in the process.

Man's need for thiamine bears a direct relation to his calorie intake and to his ingestion of carbohydrate calories in particular. The phosphorylated thiamine, or cocarboxylase, is apparently as effective as the thiamine chloride. Eddy related that when brain tissue of thiamine deficient pigeons was subjected to the breakdown of glucose to lactic acid, it was noted that there was an abnormal increase in lactic acid. It was further noted that the addition of thiamine restored tissue respiration in the presence of lactic acid, but produced no increase in the absence of the lactate. This led to a search for another intermediate — pyruvic acid. Eddy provided a brief but lucid explanation of this aspect of thiamine metabolism:

> In the conversion of glucose to carbon dioxide and water in tissue cells, one of the final steps in the process is the formation of pyruvic acid and its conversion to carbon dioxide and water by oxidation and decarboxylation. The increase in pyruvic acid in the blood of thiamine deficient individuals and its prevention by thiamine dosage suggested that B_1 fitted into the steps of glucose metabolism at the pyruvic acid stage. Beriberi cases show an increase of pyruvic acid in the circulating blood; increased blood pyruvate is today used as a diagnostic sign of thiamine deficiency.
>
> A forward step in the explanation of how B_1 might act was provided by the isolation from yeast of a coenzyme by Lohman and Schuster in 1937. This coenzyme turned out to be a cocarboxylase, in other words, the coenzyme operating with the carboxylase enzyme in splitting carbon dioxide from an organic acid such as pyruvic. Chemical analysis of this cocarboxylase proved it to be the pyrophosphate ester of B_1 or thiamine.[50]

S. Ochoa and R. A. Peters reported that there is a greater

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[50] Ibid.

amount of cocarboxylase than thiamine in animal tissue. They further stated that cocarboxylase can be synthesized from the vitamin by the liver, but not by the intestinal mucosa.[51]

B. C. P. Jansen pointed out that the discovery of cocarboxylase in yeast, and its ability to change pyruvic acid to acetaldehyde, clearly demonstrated that thiamine in the phosphorylated form played a part in yeast breakdown of sugar. Whatever the by-products between pyruvic acid and the ultimate carbon dioxide and water, thiamine pyrophosphate is an essential factor in the transformation. Inadequate supply of thiamine results in failure to eliminate pyruvic acid and failure to complete the final steps of glucose conversion into energy.[52]

This failure, of the metabolism of a fuel in a tissue, according to Eddy, "is bound of itself to cripple the full efficiency of that tissue. Secondarily, regions innervated by nerves so affected will necessarily fail to get normal control, producing results which vary with the tissue or organs so affected."[53]

The information offered above forms the basis of the thiamine rationale important to the present study. A review of the experimental use of thiamine will reveal further possible relationship between it and the neurology of speech.

A study by W. M. Govier, which considered the rationale of

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[51] S. Ochoa and R. A. Peters, "Synthesis of Cocarboxylase," Nature, 142 (1938), 358.

[52] B. C. P. Jansen, "The Physiology of Thiamine," Vitamins and Hormones, VII (1949), 83.

[53] Eddy, What Are the Vitamins?, op. cit.

vitamin therapy with cases of shock and anoxia, would seem to contribute relevant data and information basic to the comprehension of thiamine rationale.[54] Shock was induced in a number of dogs by fractional bleeding and thiamine administered to half of them with an apparently beneficial result. "The thiamine treated dogs lived longer than did the controls."[55] This result led the author to consider whether the thiamine was acting in its normal manner as a coenzyme in tissue metabolism because an animal in shock was in some way thiamine deficient, or whether the thiamine was acting in some other manner. According to Govier, "A diagnostic test well known to clinicians is the estimation of the level of pyruvic acid in the blood . . . since breakdown of pyruvic acid requires phosphoylated thiamine or cocarboxylase as a coenzyme, a deficiency of thiamine will cause pyruvate to pile up in the circulating blood."[56] Blood pyruvate determinations were done on a number of animals in shock, and the pyruvate level of the circulating blood was seen to rise from a normal amount of 1.0 to 2.0 mg. per hundred cubic centimeters to 4.0 or 5.0 mg. per hundred cubic centimeters of blood. This level is actually that seen in most cases of beriberi. The author concluded that "either these animals became thiamine deficient as shock was induced, or that their thiamine became

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[54] W. M. Govier, "Rationale for Use of Vitamins in the Therapy of Shock and Anoxia," J. Am. Med. Assoc., 126 (1944), 749-50.

[55] Ibid.

[56] Ibid.

incapable of functioning in a normal manner."[57] For an insight into some of the mechanisms involved, further direct reference would seem justified.

> It was mentioned before that the intermediate group of dogs, having normal plasma thiamine levels, were benefited by thiamine therapy. One explanation of this fact would be that the animals' own tissue thiamine became ineffective. I have also mentioned that the thiamine must be phosphorylated to diphospho-thiamine or cocarboxylase in order to be effective as a coenzyme in pyruvate metabolism. In the tissues there is probably an equilibrium between thiamine (and/or its monophosphate) and cocarboxylase as shown in this reaction:
>
> Thiamine + Phosphate ⟷ Cocarboxylase
>
> Under normal conditions most of the thiamine is in the phosphorylated form, but it seemed possible that under abnormal conditions, such as in shock, the carcoboxylase might become dephosphorylated, thus shifting the equilibrium to the left and concomitantly reducing the amount of metabolically "active" thiamine. Ochoa has shown in vitro that under anaerobic conditions such breakdown of cocarboxylase does occur, probably by means of a phosphatase. We have confirmed his results. Both cocarboxylase and total thiamine were determined in the skeletal muscle, liver and duodenum of dogs before and after shock, and after thiamine therapy. Dephosphorylation of cocarboxylase occured in 92 per cent of the cases in the muscle, in 69 per cent of the cases with duodenum and in 46 per cent of the liver samples. The magnitude of the dephosphorylation was variable, there being some tendency for more dephosphorylation to occur in dogs which went into shock with relatively small amounts of bleeding. These results have been confirmed by Alexander.
>
> Thus these animals, although well supplied with thiamine, were in a sense vitamin B_1 deficient, since their thiamine was in a form which was useless in tissue metabolism. Administration of more thiamine in large doses to these dogs as treatment resulted in resynthesis of cocarboxylase. Large doses of thiamine are probably required in order to raise the intracellular concentration of thiamine so that resynthesis may occur, even when oxidative processes supplying energy for phosphorylation of thiamine are greatly reduced.[58]

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[57] Ibid.

[58] Ibid.

DeCaro and co-workers examined the content of lactic and pyruvic acids in blood and tissues of normal and thiamine deficient rats after injections of pyruvate and lactate. Intraperitoneal injection of 0.5 to 1.0 mg. of sodium lactate per g. bodyweight caused an increase in the lactic acid content of the blood and muscles of normal rats and of rats deprived of vitamin B_1, and a slight increase in pyruvic acid content in the muscle and brain of normal rats. Similar injections of sodium pyruvate were followed by an increase in the lactic acid content of normal muscle and of blood, muscle and brain of deprived rats, and an increase in the pyruvic acid content of the muscle and brain of normal rats, and of the blood, muscle and brain of deprived rats.[59]

The disease complex that includes megaesophagus (cardiospasm) megacolon, and mega-ureter is considered by E. Etzel to be due to a chronic vitamin B_1 deficiency. The deficiency causes a degeneration of the cells of Auerbach's plexus with a resulting achalasis of the sphincters concerned. A further study of 170 cases with sixteen autopsies confirmed this conclusion. A statistical review of 621 cases observed in the last eighteen years, showed that the disease occurred at all ages, but that the majority of persons affected were young farm laborers between the ages of fifteen and twenty-five years from the poor, central and northeastern part of the State. The diet

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[59] L. DeCaro, et. al., "The Content of Lactic and Pyruvic Acids in Blood and Tissues of Normal and Vitamin B_1 Deficient Rats After Ingestions of Pyruvate and Lactate," Boll. Soc. Ital. Biol. Sper., XV (1940), 518-20.

was mainly of beans, polished rice, manioc flour and crude cane sugar, with occasionally supplements of dried meat, eggs, potatoes, vegetables and milk. Such a diet is deficient in vitamin B_1, and this fact, together with the marked susceptibility to the disease of young males, with their high caloric requirements and, therefore, high vitamin B_1 requirements, is considered as further evidence of the importance of vitamin B_1 in the etiology of this disease complex.[60]

In metabolism experiments with rats, Hermann found that during deprivation of thiamine the oxygen consumption fell markedly, declining most rapidly in the terminal stages of deficiency with the onset of inanition.[61]

A study by L. L. Hardt and E. V. Still of the thiamine content of sweat revealed considerable loss of thiamine in sweat which might have serious physiological consequences for workers and athletes with an inadequate intake of the vitamin.[62]

E. Sarfy reported that in pigeons deprived of vitamin B_1 there was an increase in the adrenalin content of the adrenals in the early stages of deficiency, but a great decrease as symptoms of beriberi began to appear. The adrenalin content of the blood of deprived pigeons was lower than normal in the first two weeks on the deficient

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[60] E. Etzel, "May the Disease Complex that Includes Megaesophagus (cardiospasm), Megacolon and Mega Ureter Be Caused by Chronic Vitamin B_1 Deficiency?", Amer. J. Med. Sci., CCIII (1942), 87-100.

[61] B. Hermann, "Vitamin B_1 Deficiency and Oxygen Consumption in Rats," Hoppe-Seyler's Ztschr., CCXXII (1941), 23.

[62] L. L. Hardt and E. V. Still, "Thiamine in Sweat," Proc. Soc. Exp. Biol. Med., XXXVIII (1941), 704-07.

diet and later much above normal. Similar changes were observed in the adrenalin content of rats deprived of vitamin B_1. When pigeons were given 1 mg. of vitamin B_1 daily, there was a decrease in the adrenalin content of the adrenals and an increase in blood adrenaline up to ten days of the over-dosing, but if the large doses were continued, the adrenalin content of the adrenals rose to normal and the blood adrenalin fell, though not to normal.[63]

An experiment by S. Ochoa was concerned with further determining enzymic synthesis of cocarboxylase in animal tissues. A summary of his findings is presented below:

1. Liver slices, lirei or "dispersions" from avitaminous pigeons convert added vitamin B_1 into cocarboxylase to an extent which does not greatly surpass the normal cocarboxylase content of the tissue. Optimally, with small amounts of vitamin, 30 per cent of this may be converted into cocarboxylase in 30-60 minutes at 38°.

2. Brain and muscle preparations are much less active; preparations from duodenal mucosa (pig) showed no activity under various experimental conditions.

3. With liver, synthesis is dependent on an active respiration and is highest at alkaline reactions (optimum about pH8.5). The synthesis is inhibited by iodoacetic acid but not much affected by NaF.

4. An essential part of the enzyme catalysing the synthesis is soluble.

5. Soluble enzymes which, when no respiration is possible, destroy cocarboxylase, are present in liver, kidney, muscle and brain; their activity is highest in those tissues (liver and Kidney) which also show the highest synthetic capacity.[64]

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[63] E. Sarfy, "The Effect of Vitamin B_1 on the Adrenaline Content of the Adrenal Glands and Blood," Hoppe-Seyler's Ztschr., CCLXII (1939), 87-94.

[64] S. Ochoa, "Enzymic Synthesis of Cocarboxylase in Animal Tissues," Biochem. J., XXXIII (1939), 1262-70.

Emmett Holt, Jr. determined the thiamine requirements of normal infants by use of a urinary excretion procedure which involved finding the intake that would maintain urinary excretion at the upper limit of the zone of minimum excretion. The requirement varied between 0.14 mg. and 0.20 mg. per day in the seven subjects studied.[65] The thiamine requirements of pre-school children were considered by H. Oldham to be 0.50 mg. per 1,000 calories.[66] Williams and co-workers described the lowest minimum thiamine requirement of man as being 0.45 mg. per 1,000 calories.[67] The concept of minimum food requirement was defined by Holt as "that intake which will just protect against definite clinical symptoms."[68] He provided a concise insight into the limitations of assessing vitamin requirements:

> The problem of assessing vitamin requirements has been complicated by the discovery of a number of variable factors which may influence them. Vitamin requirements are conditioned by pathological processes which affect absorption or utilization or increase the need for particular factors. But even in the normal subject there are wide fluctuations in requirements, caused by the nature of the food, its effect on the bacterial synthesis of vitamins in the intestine, and its content of anti-vitamins. Alterations in the diet or bacteriostatic drugs are known to affect the synthesis of vitamins in the intestine. Vitamins present in the diet may be destroyed

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[65] Emmet Holt, Jr., et. al., "The Thiamine Requirement of the Normal Infant," J. Nutrition, XXXVII (1949), 53-66.

[66] H. Oldham, et. al., "A Study of the Riboflavin and Thiamine Requirements of Children of Preschool Age," J. Nutrition, XXVII (1944), 435-46.

[67] R. D. Williams, et. al., "Observations on Induced Thiamine Deficiency in Man," Arch. Int. Med., LXVI (1940), 785-99.

[68] Holt, "The Thiamine Requirement of the Normal Infant," op. cit.

> before ingestion by exposure, processing or cooking, and in the intestine they may be rendered unavailable by agents which compete with, combine with, absorb or destroy them.[69]

Holt also described his preference for methods of determining thiamine deficiency:

> Thiamine deficiency has been measured by assays of thiamine in biopsied tissues, by determination of thiamine in serum, by the cocarboxylase level of the blood cells, by the pyruvate levels or the pyruvate; lactate ratio of the blood serum, and by various excretion procedures for measuring urinary thiamine. The biopsy technique, aside from obvious objections, is undesirable because of its inaccuracy and the paucity of "normal" standards. Pyruvate levels and Pyruvate: lactate ratios are influenced by non-specific factors (exercise, excitement) which are difficult to control in infants and were therefore to be avoided. The analytical methods for blood thiamine and cocarboxylase measurement at the time our study was begun were not considered sufficiently reliable and accurate, and some urinary excretion procedure therefore seemed the best method for estimating the degree of deficiency.[70]

W. W. Wainio reported that thiamine requirement appeared to be lower with a diet containing much protein.[71]

R. C. Wright and E. M. Scott supported the view that, with a high-fat diet, lack of thiamine is less serious because the normal oxidation of fat, unlike that of carbohydrate, by-passes the oxidation of pyruvate.[72]

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[69] Ibid.

[70] Ibid.

[71] W. W. Wainio, "The Thiamine Requirement of the Albino Rat as Influenced by the Substitution of Protein for Carbohydrate in the Diet," J. Nutrition, XXIV (1942), 317-29.

[72] R. C. Wright and E. M. Scott, "Pyruvate and Aketoglutarate Metabolism in Thiamine Deficiency," J. Biol. Chem., CCVI (1954), 725-33.

Experiments with rats weighing from 55 g., deprived and not deprived of thiamine, and with some of them subjected to paired feeding, showed that only deprivation of vitamin B_1 had any effect in causing a rise in blood pyruvic acid.[73]

Although there appear to be several questions concerning the effect of thiamine on the nervous system which are still unanswered, many recent studies have contributed both accumulative data and interesting theories. According to A. von Muralt, several hypotheses have been put forward regarding the participation of specific chemical substances in the action potential. He claimed to have brought together at least three such "action substances," acetylcholine, thiamine, and potassium. A very small quantity of acetylcholine appears to be liberated in nerves during the passage of the impulse. About ten times as much thiamine (located in the sheath) is also formed. It is believed by von Muralt that "acetylcholine formation is essential for the excitation or recovery process and that aneurin (thiamine) is a reservoir substance closely connected with the formation and disappearance of acetylcholine."[74] F. Wyss claimed that like acetylcholine, thiamine is supposed to exist in two forms, bound and free. He considered it to be of general agreement that thiamine is concerned in the formation of acetate from pyruvate.[75] Von Muralt found that on mild oxidation of

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[73]G. Ferrari, "Behavior of Blood Pyruvate in Undernutrition," Boll. Soc. Ital. Biol. Sper., XXIX (1953), 290-92.

[74]A. von Muralt, "Chemical Intermediate in Nerve Action," Nature, CLIV (1944), 767.

[75]F. Wyss, "The Two Forms of Acetylcholine and Thiamine," Helv. Physiol. Acta., II (1944), 121.

nerve with ferricyanide in an alkaline medium, thiamine is changed to thiochrome and longitudinal or cross sections of nerve show an intense violet fluorescence of the myelin sheaths. In degenerating nerves of guinea pigs a decrease in thiamine content can be detected by this method within twenty-four hours after section.[76]

In a later article, von Muralt stated, ". . . thiamine is essential for the maintenance of the internal chemical equilibrium of the neurons (nerve cell and peripheral nerve). The store of thiamine in the cell is continuously used up in maintaining this equilibrium, and, as the cell is not able to synthesize this vitamin, a constant requirement from other sources is the result."[77] In consideration of what is the role of thiamine in the chemical equilibrium of the neurone, why is thiamine permanently used up in maintaining this equilibrium, and what is the requirement of a neurone at rest and during activity, von Muralt admitted that these questions seemed so simple and yet were so difficult to answer with even a first approximation of the problem.

The extracts of fifty frozen nerves (fifty excited and fifty unexcited) were fed to various groups of rats in a state of avitaminosis. The average increase of pulse rate after extract feeding revealed that the extracts from stimulated nerves contain a measurable amount of thiamine, whereas the extracts of unstimulated nerves contain only a

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[76] von Muralt, "Chemical Intermediate in Nerve Action," op. cit., 768.

[77] A. von Muralt, "Thiamine and Peripheral Neuro-physiology," Vitamins and Hormones, V (1947), 114-15.

subthreshold amount of thiamine, if any, according to von Muralt.[78] Thiamine is liberated in ten to twenty times greater amounts than acetylcholine and especially is this true during excitation. The preceding statements were repeatedly stressed in von Muralt's report. It was observed by Wyss and Wyss that after poisoning a nerve with monoidoacetic acid, more thiamine is obtained in the extract of resting nerves than in the extract of excited nerves. In the poisoned nerve thiamine is liberated in the resting metabolism and "fixed" in the process of excitation (under conditions in which the sequence of chemical reactions has been altered by the poisoning, the poisoned nerve shows a behavior opposite to that of the normal nerve).[79]

D. Nachmansohn and H. B. Steinbach studied the axone of the squid and found that cocarboxylase is concentrated on the surface of the axone. If the nerves are in electrotonus at the moment of fixation, an accumulation of thiamine is observed at the site of the anode, which is an indication that thiamine is liberated in relation to anabolic, rather than to catabolic, processes.[80] These findings would seem to support von Muralt in his view that thiamine plays an important role in nerve metabolism and that "during the state of liberation, or shortly afterwards, a certain liberation of thiamine takes place which

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[78] A. von Muralt, "Stimulated and Unstimulated Nerve Content of Thiamine," Arch ges. Physiol., CCXXXVII (1943).

[79] A. Wyss and F. Wyss, "Comparison of Extractions of Thiamine from Poisoned and Excited Nerves," Experientia, I (1944), 160.

[80] D. Nachmansohn and H. B. Steinbach, "Thiamine Concentration in Squid Axone," J. Neurophysiol., V (1942), 109.

disappears almost as quickly as it is produced."[81] It was emphasized that the experimental findings were fragmentary and their evaluation might be influenced by further experimental work.

P. Kaiser mentioned that thiamine inhibits the action of acetylcholine on the heart: "Assuming that normally this action counterbalances the action of acetylcholine (which is liberated as a result of the natural action of the vagus), then a state of avitaminosis should produce bradycardia."[82] Williams and colleagues observed this in man at the first stages of avitaminosis.[83]

The content of thiamine was studied by von Muralt and J. Zemp in the frog sciatic nerve. Stimulation significantly increases the value of thiamine.[84]

C. Casella and L. G. DeCaro pointed out that even when grave neurological signs of thiamine deficiency are present, the rate of conduction and action potential are normal in the sciatic nerve.[85]

Another recent investigation in this area was reported by W. A. Mannell and R. J. Rossiter. They reported:

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[81] A. von Muralt, "Chemical Intermediate in Nerve Action," op. cit., 768.

[82] P. Kaiser, "Thiamine and Acetylcholine in Bradycardia," Arch. ges. Physiol., CCXXXXII (1944), 504.

[83] R. D. Williams, et. al., "Induced Thiamine Deficiency and the Thiamine Requirement of Man," Arch. Internal Med., LXIX (1942), 725.

[84] A. von Muralt and J. Zemp, "Thiamine Content in Frog Sciatic Nerve," Arch. ges. Physiol., CCXXXXVI (1943), 746.

[85] C. Casella and L. G. DeCaro, "Conduction and Action Potential of Nerves of Rats Deprived of Vitamin B_1," Arch. Sci. Biol., XXXVII (1953), 229-36.

Rats received for 44 days an adequate basal diet or one deficient in vitamin B_1. In some rats the sciatic nerve was cut and, after eight days, the concentration of nucleic acid and phospholipin in intact and degenerating nerve was estimated. The values were compared with those for animals of the same age receiving adequate vitamin B_1, called age controls, for younger animals receiving adequate diet but killed when the bodyweight was the same as in deprived rats, called weight controls, and for animals of the same age receiving adequate diet restricted in amount, called weight and age controls.

In the age controls concentrations of nucleic acid and phospholipin in nerve tissue decreased with increasing age and bodyweight, and the previous observation was confirmed that, in the intact sciatic nerve of the rat, the concentration of nucleic acid was characteristic of age but not of bodyweight, and the concentration of phospholipin was characteristic of bodyweight but not of age. In rats deprived of vitamin B_1, the concentration of nucleic acid was less than in the weight controls, but did not differ from that in the weight controls but were greater than in the age controls.

After section of the sciatic nerve, increase in the concentration of nucleic acids occurred more slowly in rats deprived of vitamin B_1 than in the weight controls, which were younger animals, but at the same rate as in the other two sets of controls. The decrease in concentration of phospholipin in nerves from deprived animals took place more slowly than in nerves from any control. The result distinguished the effects of vitamin B_1 deficiency from those of lack of protein or of total calories.

There was no evidence that during degeneration of the sciatic nerve proliferating Schwann cells provided enzymes which destroyed the myelin sheath, since there was no destruction of myelin or loss of myelin lipids.[86]

Vitamin B_1 and acetylcholine formation in isolated brain matter was examined by P. J. Mann and J. H. Quastel. Their findings are summarized below.

No appreciable differences were found in the capacity of intact brain slices, from normal and polyneuritic pigeons, to synthesise acetylcholine under suitable aerobic conditions in a bicarbonate Locke pyruvate medium. If, however, a

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[86] W. A. Mannell and R. J. Rossiter, "Effect of Thiamine Deficiency on the Concentration of Nucleic Acid and Phospholipid in Intact and Sectioned Nerves," Brit. J. Nutrition, VIII (1954), 56-64.

> medium containing a relatively high concentration, 0.03 M, of potassium ions was used, the polyneuritic pigeon brain synthesised acetylcholine at a rate less than the normal, but this was increased to normal by addition of vitamin B_1. No such increase occurred when the vitamin was added in similar circumstances to slices of normal pigeon brain. The presence of vitamin B_1 affected the synthesis of acetylcholine by polyneuritic brain only in the presence of pyruvate.[87]

Thiamine was ascertained in the cerebrospinal fluid by G. Saker by means of the Phycomyces test. The amount of vitamin B_1 present was very variable and bore no relation to the amount present in the blood or to the clinical condition of the patient. Intravenous injection of vitamin B_1 was followed by an increase in the amount found in the cerebrospinal fluid; vitamin B_1 rapidly passed into the blood when injected intrathecally.[88]

M. Prados and R. L. Swank reported an investigation of vascular and interstitial cell changes in vitamin deficient animals. In pigeons and kittens made chronically or acutely deficient in thiamine, a study was made of the vascular lesions in the brain. Vasodilation, probably caused by increased permeability of the vessels due to accumulation of metabolites from disturbed carbohydrate metabolism and consequent collection of fluid and red cells in the perivascular spaces, was the first sign of damage, and infiltration of the surrounding tissue followed. The distribution of the vascular lesions corresponded with that of degenerating neurones. Neuronal lesions were always found

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[87] P. J. Mann and J. H. Quastel, "Vitamin B_1 and Acetylcholine Formation in Isolated Brain," Nature, CXXXXV (1940), 856-57.

[88] G. Saker, "Aneurin in the Cerebrospinal Fluid," Klin. Wochenschr., XIX (1940), 99-102.

surrounding hemorrhages. Swelling of the oligodendrocytes and clasmatodendrosis of astrocytes were observed in the brains of kittens with acute deficiency symptoms, but in kittens with chronic deficiency, the oligodendrocytes were almost unchanged and the astrocytes became hyperplastic and hypertophied. These changes were considered to be non-specific and related to the gliosis which occurs when neurones die. It is not thought that vitamin B_1 has specific anti-degenerative properties for nervous tissues.[89]

Unlike other tissues studied by J. Salcedo and co-workers, the brains of rats maintained their thiamine concentrations in the face of a deficit of thiamine for a considerable period, after which there occurs an abrupt fall in thiamine content. The critical point at which the brain begins to lose its thiamine corresponds to the attainment of the minimum level of urinary thiamine excretion. This finding would seem to support the view that the point of urinary excretion is of physiological significance. The authors suggested that the point of minimum excretion in the urine is a highly useful criterion for measuring thiamine requirements under various conditions.[90]

Functional studies of the nervous system in experimental beriberi conducted by C. F. Church appear to furnish directly related material. A summary of his work is presented below.

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[89] M. Prados and R. L. Swank, "Vascular and Interstitial Cell Changes in Thiamine-Deficient Animals," Ach. Neurol. Psychiat., XXXXVII (1942), 626-44.

[90] J. Salcedo, Jr., et. al., "The Relation Between Urinary Excretion and Tissue Concentrations of Thiamine in Rats," J. Nutrition, XXXVI (1948), 307-13.

1. The characteristic neurologic symptoms of beriberi resulting from lack of vitamin B (B_1) in the rat are 1, changes in muscular tonus; 2, ataxia; 3, disturbances of equilibrium; and 4, hyper-excitability. Muscular tremors and weakness sometimes occur but true convulsions and paralysis are not part of the beriberi syndrone.

2. The labyrinthe righting reflex is lost in beriberi at the onset of disturbances of equilibrium, but the neck and body righting reflexes are preserved. A pathologic tail reflex exhibited by beriberi rats gives evidence of the spreading of the reflex arc in the spinal cord.

3. Evidence is presented of the functional integrity of the peripheral nerves and proprioceptive nerve endings in beriberi in the rat by the method of recording nerve action potentials.

4. Vestibular function is significantly altered in beriberi. The duration of nystagmus following a standardized rotational stimulus increases progressively following withdrawal of vitamin B (B_1) from the diet, preceding the appearance of other neurologic symptoms.

5. This prolongation of vestibular response is characteristic of vitamin B (B_1) deficiency. Inanition, otitis, and deficiency of vitamin D do not appreciably affect the mean result of the vestibular test, while deficiency in vitamin A diminishes the result. In vitamin G (B_2), a small terminal increase was noted.

6. The vestibular function test is sensitive to the relative insufficiency of vitamin B (B_1) resulting from depriving the animal of fat (with its "sparing action" upon vitamin B.)

7. The chief neurologic manifestations of beriberi in the rat can be accounted for on the basis of lesions in the vestibular nuclei. The finding of perivascular hemorrhages in this region is confirmed but these lesions are regarded as secondary to insidious tissue changes resulting from specific lack of vitamin B (B_1).[91]

Injection of 0.1 to 0.2 ml. of a 0.2 per cent solution of lactic or pyruvic acid into the brains of pigeons produced convulsions similar

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[91] C. F. Church, "Functional Studies of the Nervous System in Experimental Beriberi," Am. J. Physiol., III (1935), 660.

to those observed in birds deprived of vitamin B_1. The effect was apparently specific for lactic and pyruvic acid as the injection of similar amounts of physiological salt solution or of larger amounts of sodium acetate produced no convulsions. These observations by I. I. Nitzescu and C. Angelescu, are taken as further evidence of the effect of accumulation of pyruvic and lactic acids in the brain in causing acute symptoms of vitamin B_1 deficiency.[92]

R. R. Swank and H. H. Jasper observed that when pigeons were deprived of thiamine, there was a progressive increase in the amplitude of the potentials recorded by the encephalogram up to about three times the normal value. In the final stages of deficiency, there was marked slowing down and depression of brain potentials. If vitamin B_1 was administered, the brain potentials returned to normal within a few hours. It was suggested that the changes in brain potentials indicate marked facilitation of cortical discharge during the initial phases of vitamin B_1 deficiency before depression occurs.[93]

Histopathological studies were reported by Swank upon pigeons subjected to total or partial thiamine deprivation, to starvation alone, or to starvation and deprivation of thiamine. The state of acute deficiency was manifested by opisthotonos. Few or no morphological

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[92] I. I. Nitzescu and C. Angelescu, "Methods for Causing Convulsions Similar to Those Seen in Polyneuritis by Intracerebral Injection of Lactic or Pyruvic Acid," Ztschr. Vitamin forsch., XLL (1942), 82-85.

[93] R. R. Swank and H. H. Jasper, "Electroencephalograms of Thiamine-Deficient Pigeons," Arch. Neurol. Psychiat., XXXXVII (1942), 821-27.

changes were detected in acute cases, but in chronic cases, a degeneration of both peripheral and spinal neurons was demonstrated. The extent of degeneration of sciatic nerve fibers corresponded closely with the degree of paralysis observed. Further studies of thiamine deficiency in pigeons were made with diets described above giving acute and chronic symptoms. Histological examination was made of the brains of seventy deprived pigeons and of normal birds, by various methods of fixing and staining designed to demonstrate the neurofibrillar structure of the neuron. The first visible change in the neuron was a degeneration of the distal part of the axon, moving towards the center and accompanied by slight shrinkage of the cells. Large nerve fibres degenerated first, medium sized ones, later, while the small fibres usually remained intact even in severe deficiency. Birds with marked opisthotonos sometimes showed no neurological lesions. Study of opisthotonos in acutely deficient birds indicated that the movement was probably due to selective release of vestibular centers from labyrinthine control. In chronic vitamin B_1 deficiency, pigeons without opisthotonos showed moderate degeneration of all central and peripheral terminations of vestibular nerves. In both acute and chronic states of deficiency there was no consistent degeneration in the optic lobes, the nucleus rotundus of the thalamus, the reticular formation or the secondary vestibulo-cochlear centers.[94]

From curative studies it appeared that neurons showing early

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[94] R. L. Swank, "Avian Thiamine Deficiency," J. Exp. Med., LXXI (1940), 683-702.

degeneration changes could be restored to normal by administration of vitamin B_1, but that severely affected ones continued to degenerate. Brain hemorrhages observed in some birds were apparently secondary to changes in axons and cell bodies, and had no relation to the clinical condition according to work by Swank and Prados.[95]

J. M. Cooperman's study on the influence of thiamine on the susceptibility of chicks to avian encephalomyelitis is summarized below.

> One-day old leghorn chicks, divided into three groups, receiving low, suboptimum, and optimum level of thiamine were inoculated with a virus suspension of avian encephalomyelitis. The chicks receiving the highest level of thiamine were protected to the greatest degree.
>
> In another series of one-day old white leghorn chicks were given an optimum level of thiamine in the ration for two weeks, then divided into three groups receiving levels of thiamine as indicated in the previous experiment for two weeks, at the end of which time they were inoculated. In this case all the chicks receiving the lowest level of thiamine were protected to the greatest degree.
>
> It is evident that the protection afforded against this virus depended upon a number of factors, which included the age of the chick, the previous state of nutrition and the state of nutrition at the time of inoculation.[96]

S. Stone studied the effectiveness of thiamine therapy in several degenerative and infectious disorders of the nervous system, such as tabes dorsalis, neurosyphilis, and poliomyelitis. Intraspinal pyridoxine and thiamine therapy, (in combination with artificial fever in about half the cases), resulted in an improved feeling of

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[95] R. L. Swank and M. Prados, "Avian Thiamine Deficiency 2," Arch. Neurol. Psychiat., XXXXVII (1942), 97-131.

[96] J. M. Cooperman, et. al., "The Influence of Thiamine on the Susceptibility of Chicks to Avian Encephalomyelitis," J. Bact., LII (1946), 467.

well-being, increase in performance ability, and greater range of movement in the affected extremities. Treatment was more effective in patients with weakness on effort and muscle cramps but showing little muscle atrophy, and also in patients with some residual muscle power. On the other hand, chronic cases of poliomyelitis with no muscle power, or only a little, exhibited no significant change in strength of defected muscles.[97]

The influence of exercise on the growing rat in the presence and absence of vitamin B_1 was investigated by N. B. Guerrant and R. A. Dutcher. Forced exercise in rats deprived of vitamin B_1 reduced the food intake and growth rate, and accelerated the onset of paralytic symptoms. In rats receiving vitamin B_1, forced exercise reduced the growth rate and increased the number of faecal pellets excreted. The animals that were confined without exercise showed slightly greater food consumption and excreted greater quantities of faeces than exercised rats. The onset of paralysis was slower in confined rats deprived of vitamin B_1 than in exercised animals. These findings did not resemble those with animals deprived of vitamin A, but the differences might be explained by the differences in the physiological functions of the two vitamins.[98]

The work output of frog muscles was increased by additions of

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[97] S. Stone, "Pyridoxine and Thiamine Therapy in Disorders of the Nervous System," Nutrition Reviews, IX (May, 1951), 131.

[98] N. B. Guerrant and R. A. Dutcher, "The Influence of Exercise on the Growing Rat in the Presence and Absence of Vitamin B_1," J. Nutrition, XX (1940), 589-98.

thiamine hydrochloride or additions of thiamine pyrophosphate, in a study by N. W. Shock and W. H. Sebrell.[99]

Performance in endurance tests of holding the arms horizontal or holding the breath for prolonged periods did not appear to be affected by administration of vitamin B_1. Psychological factors were shown to influence the tests which were, therefore, not considered to give reliable indication of muscular control, according to the investigators P. V. Karpovich and N. Millman.[100]

W. Croese reported the effect of administering vitamin B_1 and glucose in acute experimental exhaustion in different human subjects on the bicycle ergometer. A combination of vitamin B_1 and glucose was highly effective. In vitamin B_1 deficiency, administration of glucose alone had no effect, but benefit accrued as soon as vitamin B_1 also was administered. This was suggested as a method of demonstrating vitamin B_1 deficiency. An increased requirement for vitamin B_1 during work at high temperatures was also demonstrated, depending possibly on increased excretion of vitamin B_1 or cocarboxylase in the sweat.[101] In another article Droese stated that, "maximum work which can be produced by human subjects is increased by the addition of thiamine. Metabolic

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[99] N. W. Shock and W. H. Sebrell, "Relation Between Thiamine and Co-carboxylase Concentration and Work Out-put of Perfused Frog Muscles," Proc. Soc. Exptl. Biol. Med., LIX (1945), 212-17.

[100] P. V. Karpovich and N. Millman, "Vitamin B_1 and Endurance," New Engl. J. Med., CCXXVI (1942), 881-82.

[101] W. Droese, "The Effect of Vitamin B_1 and Glucose on Acute Experimental Exhaustion," Arbeits. Physiol., XI (1940), 117-28.

rate and efficiency are not influenced."[102]

W. W. Tuttle reported that the reaction time of hypo-vitaminotic women was longer than those with adequate thiamine consumption.[103]

It was reported by R. F. Harrell that thiamine increased or improved acuity of vision, skill at games, reaction time, reading, arithmetical processes, memorizing, and intelligence. Her procedure involved the administration of 2 mg. per day of thiamine to thirty-seven children and a placebo to thirty-five carefully matched controls.[104]

Harrell's findings would seem to be at least partly contradicted by this summary of a study by O'Shea and colleagues:

> From observation on four adult subjects and four controls we may conclude:
>
> 1. Foresight and judgment, as measured by performance on maze tests, are impaired when the subjects are deficient in the B vitamins and are improved after therapy with thiamine or with the B complex.
>
> 2. General intelligence, reasoning, ability (reading), and speed of hand muscle coordination (tapping) show no measurable deterioration when the subjects are deficient in the B vitamins and no improvement after therapy with thiamine or with the B complex.[105]

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[102] W. Droese, "The Effect of a Mixture of Vitamin B_1 and Glucose on Physical Efficiency," Munch. Med. Wochenschr., LXXXVIII (1941), 909.

[103] W. W. Tuttle, et. al., "The Effect of Low Thiamine Intake on the Reaction Time of Women," Federation Proc., VII (1948), 126.

[104] R. F. Harrell, "Mental Response to Added Thiamine," J. Nutrition, XXXI (1946), 283-98.

[105] H. E. O'Shea, et. al., "Mental Changes in Experimental Deficiency," Am. J. Med. Sci., CCIII (1942), 396.

E. C. Robertson conducted a carefully controlled investigation patterned after the study of Harrell. Robertson used identical twins as subjects and controls, and found no significant changes that could be attributed to thiamine supplement.[106]

In view of the purpose of the present investigation, and the studies mentioned above relating nutrition to behavior, it seems interesting to take notice of a pronouncement by the Nutrition Foundation, Inc., which appeared in the August, 1954 issue of Nutrition Reviews:

> The complex interrelationships between nutrition and behavior represent an interesting but underdeveloped sector of the science of human nutrition . . . .
>
> The effects of nutrition represent phenomena challenging modern social science by the need for combining the approaches of anthropology, sociology, and psychology. The problem of nutrition and psyche can and must be approached from the somatopsychologic point of view (effect of nutrition on behavior), as well as by considering the emotional significance of foods and eating to the individual and to the group.[107]

It seems advisable at this point to consider further the theoretical rationale upon which the use of thiamine for stuttering or nonfluency is based. Lester Hale summarized:

> The central nervous system depends upon carbohydrate as a source of energy and thiamin is needed in carbohydrate metabolism. When there is a reduction in normal thiamin intake, the central nervous system is likely to suffer. Conversely, if added strain is placed upon the nervous system,

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[106] E. C. Robertson, "The Effect of Added Thiamine on Growth, Vision, and Learning, Using Identical Twins," J. Nutrition, XXXIV (1947), 691-700.

[107] The Nutrition Foundation, Inc., "Nutrition and Behavior," Nutrition Reviews, XII (August, 1954), 237-40.

> or there is a greatly augmented metabolism, there is increased thiamin requirement. If normal thiamin intake is not sufficient to meet these conditions or thiamin is being inadequately assimilated, neurological imbalance may result.[108]

Louis Goodman and A. Gilman point out that symptoms of mild thiamine deficiency are not as characteristic as severe deficiency and may escape diagnosis.[109] Hale emphasized that thiamine deficiencies may exist without outward manifestations until circumstances of additional stress are placed on the system. He postulated that "A residual diathesis may exist in the thiamin level, and this accounts in part for the narrow margin of safety in some individuals who seem predisposed to stutter."[110]

Hale's comments on the effect of "stress" upon the individual appear to be particularly relevant to a recent discussion of this topic by Benjamin Ershoff:

> Any factor that interferes with the digestion, absorption, or utilization of nutrients, or increases their destruction or excretion may result in malnutrition despite the apparent adequacy of the diet fed. Body requirements for essential nutrients may furthermore be significantly increased for purposes of detoxification or by factors such as physical exertion, fever, drugs, toxins, burns, fractures, and other trauma, major surgical procedures, abnormal environmental conditions and others. The net result of such factors is an increased body requirement beyond the usual or average range and the precipitation of nutritional deficiencies on diets that would otherwise be adequate.

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[108] Lester L. Hale, "A Consideration of Thiamin Supplement in Prevention of Stuttering in Preschool Children," JSHD, XVI (December, 1951), 328-29.

[109] Louis Goodman and A. Gilman, The Pharmacological Basis of Therapeutics (New York: MacMillan, 1941).

[110] Hale, "A Consideration of Thiamin Supplement in Prevention of Stuttering in Preschool Children," op. cit., 330.

> . . . . It is erroneous to state that "stress" per se increases nutritional requirements, for "stress" is not a specific unvarying and distinct entity. "Stress" is a state of the organism, a resultant of those processes an organism employs in attempting to maintain homeostasis under unfavorable alterations in the environment (including the internal milieu). Furthermore, since life itself is a process in which the organism attempts to maintain itself in a changing environment, "stress" is inherent in life itself. The increased nutritional requirements following exposure to stress or agents result not as a consequence of "stress" per se, but rather from the increased requirement for specific nutrients due to the physiologic effects of the particular stress or agent involved.[111]

It is made clear by Hale that the ontogenesis of speech can be both a source of a specific stress to the individual, and it can be affected by internal as well as external untoward conditions. He stated:

> The ease and fluency of the conditioned reflexes of speech are most easily upset when the synergic movements are being first acquired as symbols of thought and feeling during the preschool age. If thiamin can be of any assistance in controlling stuttering, it is felt that it would be of most preventive value in the young child.[112]

Elizabeth R. Alexander conducted an exploratory investigation of thiamine as a stuttering preventive among pre-school children.[113] In this experiment, ten mg. of thiamine were administered three times daily to a selected group of ten pre-school children who showed beginning symptoms of stuttering. Another group of children with non-fluent

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[111]Benjamin H. Ershoff, "Nutrition and Stress," Nutrition Reviews, XIII (February, 1955), 3-4.

[112]Hale, "A Consideration of Thiamin Supplement in Prevention of Stuttering in Preschool Children," op. cit., 330.

[113]Elizabeth R. Alexander, "An Experimental Study of the Effectiveness of the Administration of Thiamin Hydrochloride in Preventing Stuttering Among Pre-School Children," op. cit., vi.

speech, from the same environment, were given a placebo during the same period of time. At the end of one month, the groups were reversed and observations of both groups continued for another month. Neither the parents nor the investigator knew which dose the child was receiving, and improvement was judged on the basis of these individuals' evaluations.

Alexander summarized her findings as follows:

1. Unquestionable speech improvement in 55 per cent of all the cases.

2. There may have been an improvement in an additional 20 per cent of the cases.

3. No improvement can be claimed in 20 per cent of the cases.

4. Of the two and three year olds in the experiment, 80 per cent were unquestionably improved.

5. Only 50 per cent of the four year olds were definitely improved.

6. It is doubtful that either of the two five year olds made much improvement.

7. There was negative evidence of the effect of thiamin on the speech pattern of the seven and eight year olds.

8. In four cases where there was regression of speech fluency occurring following the cessation of thiamin therapy, there was improvement noted again after thiamin was resumed.

9. One of the cases which was reported as unimproved during thiamin therapy, showed an increase of tensions, hesitations, and other stuttering symptoms after the thiamin had been stopped.

10. With only one exception, cases that showed marked reduction of stuttering symptoms made the improvement within the first two weeks of treatment.[114]

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[114] Ibid., 73.

Alexander concluded, "Enough evidence of improvement in sufficient numbers of cases indicates that the administration of thiamin hydrochloride may be effective in preventing stuttering in pre-school children."[115]

Several recommendations for further study were made by Alexander, and they would appear to be of extreme relevance to the current study. She suggested that future research in this area should include objective determinations of the thiamine status of the subject before and during the test dose. A further recommendation was made to the effect that methods of determining improvement be subjected to more controlled quantification.[116]

Although it is principally Alexander's study upon which the present research is based, it may be relevant to report E. M. Penson's study of the effect of thiamine on twenty adults who stutter. Using a counterbalanced thiamine-and-placebo design similar to Alexander's, Penson surmised:

> 1. No positive evidence was found that would justify a definite statement that thiamin serves as a factor facilitating speech training.
>
> 2. On the other hand, no evidence was found that would justify a definite statement that thiamin does not serve as a factor facilitating speech training.
>
> 3. The results indicate some possibility that thiamin may have contributed to speech improvement.
>
> 4. In spite of the indefiniteness of the results, there seems to be enough indication of some possible contribution

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[115] Ibid., 76.

[116] Ibid., 76-77.

of thiamin to speech improvement to warrant further investigation.[117]

This chapter has presented a brief historical background to the subject of stuttering and non-fluency. Reference has been made to studies related to the efficacy of thiamine. Investigations directly relevant to this research have been reviewed.

The purpose of the present study is to investigate the effect of thiamine on children with speech non-fluency, using the recommended additional controls of determining thiamine status through assay and dietary history, and determining speech improvement by relatively quantitative measures.

Chapter II describes the procedure followed during the course of the study, and the methods used to determine and evaluate results.

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[117] Edward M. Penson, "An Exploratory Study of the Effect of Thiamin Hydrochloride on Adults Who Stutter," (Unpublished M. A. thesis, Ohio University, 1951), 95.

CHAPTER II

DESCRIPTION OF PROCEDURE

The Subjects

The age of the children used as subjects ranged from 3.0 years to 7.1 years. The mean age was 5.015 years. The median age was 5 years, as was the mode. Dorothy Davis Tuthill, in her study of non-fluency in the speech of young children, designated two to seven years of age as the range most likely to include normally non-fluent utterance.[1] Wendell Johnson concurred with this age range.[2] The present study did not include children under three years of age, because these children were not amenable to successful urine sampling nor were they adaptable to the speech rating situations which required connected, spontaneous discourse in the absence of a parent.

There were twenty-two male experimental subjects and ten female experimental subjects in the study. Although we are dealing with non-fluent speech behavior, it may be significant that, in the present study, the sex distribution of the subjects compared favorably with national incidence estimates of stuttering in the male and female as cited in

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[1]Dorothy Davis, "The Relation of Repetitions in the Speech of Young Children to Certain Measures of Language Maturity and Situational Factors: Part I," The Journal of Speech Disorders, IV (December, 1939), 318.

[2]Johnson, People in Quandries, op. cit., 445.

the report of the White House Conference on Special Education.[3]

There were several sources from which the thirty-two non-fluent experimental subjects and twenty-two fluent control subjects were selected:

1. Subjects were referred by three pediatricians of the community for screening by a panel of at least seven trained judges who rated degrees of fluency—non-fluency on a five point scale. The panel of judges and the construction of the rating scale are described in more detail below.

2. Subjects were obtained through a "pre-screening" survey, conducted by the investigator and a co-worker, of seven private nursery schools. If a child responded appropriately during the survey, his parents were invited to have the child seen later by the fluency rating panel. A child's responses were thought to be "appropriate" for panel screening if his speech appeared to the investigator and co-worker to be either sufficiently fluent to warrant considering him as a potential fluent control subject, or sufficiently non-fluent to warrant consideration as a potential non-fluent experimental subject.

3. Subjects were obtained through a survey conducted by the investigator and co-worker of the kindergarten and first grades of four public schools. If a child responded appropriately during the survey, he was seen later by the panel.

4. Subjects were obtained through invitations extended to the

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[3]White House Conference on Child Health and Protection, Special Education, Chapter on "The Child Defective in Speech" (New York: D. Appleton-Century, 1931).

parents by the investigator, who obtained the parents' names and addresses from pre-school registration lists. If the parents accepted the invitation, the children were given appointments to be seen by the panel for fluency rating.

5. Subjects were obtained through the process of parents referring other parents to the investigator for possible inclusion in the study. The children referred in this manner were seen by the panel if they responded appropriately during the pre-screening survey conducted by the investigator and co-worker.

In this manner a total of 1,352 children were pre-screened. Of this number, fifty-seven were considered by the investigator and co-worker to be non-fluent. Forty-four of these children with non-fluent speech were seen by the panel, and in forty-one cases, the panel also considered them to be non-fluent. No experimental subjects dropped out of the study once they had started. One control subject discontinued her participation after the first week, because of her inability to digest the administered tablet.

It seems relevant to note that Davis' study found that "the average child repeated fourteen words in every thousand words he spoke . . . . There was individual variation on this measure with a number of children tending to repeat words more than the average. . . ."[4] It may appear that the present study uncovered a low incidence of

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[4]Davis, "The Relation of Repetitions in the Speech of Young Children to Certain Measures of Language Maturity and Situational Factors: Part I," op. cit., 311.

non-fluency, in view of Davis' belief that non-fluent speech is part of the speech pattern of all children at some time from their second to their seventh year.[5] However, this was not the case if one considers that many of the younger children observed may not yet have entered a relatively non-fluent period, while a large number of the older children may have already completed this non-fluent stage.

It should be clearly established that at no time during the experiment were the parents or children informed of the particular aspect of speech being studied. Only three of the parents were aware of the non-fluency aspect of the study prior to its outset, and in these instances the fathers were members of the rating panel. All other parents were informed that the study was concerned with investigating the relationship between nutrition and general speech development. Individual reports dealing with the child's general speech picture were sent to the parents.[6] After the study was completed, the parents were informed of the specific factors studied and the results were made known to them.

Dosage and Medical Approval and Prescription

In the previous study of non-fluency involving the effect of thiamine on children of this age, 10 mg. of thiamine were administered three times each day.[7] In the present investigation, it was decided

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[5] Ibid., 318.

[6] Appendix A.

[7] Elizabeth R. Alexander, "An Experimental Study of the Effectiveness of the Administration of Thiamin Hydrochloride in Preventing Stuttering Among Pre-School Children," op. cit., vi.

that a substantial increase in dosage might aid in obtaining more lucid results. It should be pointed out that orally ingested thiamine is non-toxic, even in doses which are several times larger than the usual daily intake.[8] This assurance from H. R. Rosenberg was substantiated by L. Goodman and A. Gilman:

> Toxic doses of thiamine are many thousand times greater than the therapeutic, and thus the vitamin has a very high therapeutic index. There is no reason to expect untoward reactions from even the most vigorous therapeutic regimen with thiamine.[9]

The dose used in this project was 25 mg., administered in tablet form, three times daily.

After a child was designated, by virtue of the panel's ratings, as being a potential subject, and the parents indicated their willingness to participate, the child's physician or pediatrician was contacted by the investigator. The medical doctor made one of three pronouncements: (1) the child is physically fit and can be included in the study; (2) the child has not been examined recently enough, and if the parents will permit the child to be examined, (and the findings are negative), the child can be included in the study; (3) the child's physical status does not warrant his inclusion in the study.

In addition to this precaution, a letter, containing a prescriptive and expositional statement was presented to the parents.[10] The

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[8] H. R. Rosenberg, Chemistry and Physiology of the Vitamins (New York: Interscience Publications, 1942), 169.

[9] Goodman and Gilman, The Pharmocological Basis of Therapeutics, op. cit., 1246.

[10] Appendix B.

letter was signed by Raymond S. Camp, M. D., a pediatrician of the city in which the study was conducted.

Experimental Design

By and large, the experimental design consisted of two groups of non-fluent, experimental subjects which were counterbalanced, and a third group consisting of fluent, control subjects.

Group I, consisting of sixteen non-fluent subjects, received 25 mg. of thiamine three times daily for a period of five or four weeks. This was followed by the administration of a placebo for an equal period.

Group II, consisting of sixteen non-fluent subjects, who were matched with subjects in Group I as rigidly as possible in regard to age, sex, socio-economic status, and degree of non-fluency, received the placebo during the first experimental period. During the next period, the subjects in this group received 25 mg. of thiamine three times daily.

Group III, consisting of twenty-two fluent control subjects, were matched with a non-fluent subject in the manner already mentioned.

The thiamine and placebo tablets were indistinguishable from each other in aspects of size, shape, color, texture and type of container. Because thiamine has a rather characteristic odor, several drops of flavoring such as spirit of peppermint, were applied to each bottle of thiamine and placebo.

Changes in speech symptoms or degrees of non-fluency, were determined by a panel consisting of as many as eleven, and a minimum of

seven judges. These judges were: (1) Speech Pathologists with the Ph.D. in Speech; or (2) Graduate students working toward an advanced degree with a major in Speech Pathology, who had clinical experience with stuttering and non-fluency.

At the outset of the judges' training period, a seven point scale was used.

1. Fluency relatively free from observable non-fluency.

2. "Normally" non-fluent under exciting conditions only.

3. Occasional or mild non-fluency without muscular tension.

4. Moderately severe non-fluency, accompanied occasionally by muscular tension.

5. Severe, or frequent, or consistent non-fluency, accompanied by moderately severe muscular tension.

6. Severe, or frequent, or consistent non-fluency accompanied by severe, or frequent, or consistent muscular tension.

7. Secondary of full fledged stuttering, including starters, avoidance, and hypertension.

Although agreement among the judges appeared to be high, the investigator and the judges agreed that the validity of the scale was in doubt. The high agreement had consisted, for the most part, of ratings of "point one" on the scale. After several discussions, it became clear that the phrase, "under exciting conditions only," contained in point two, served to prevent the judges from committing themselves regarding observable and consistent non-fluency. Furthermore, the factor of "muscular tension" contained in points three, four, five, and six tended to make the scale a double or "two-qualitied" one. Most

of the judges concurred with the writer to the effect that while non-fluency is an observable behavior, muscular tension must, in part, be assumed as well as observed.

For the above mentioned reasons, then, the rating scale described below was adopted and used.

1. Fluency
2. Mild non-fluency
3. Moderately severe non-fluency
4. Severe non-fluency (primary stuttering)
5. Stuttering (with secondary characteristics)

P. M. Symonds indicated that seven is the optimal number of steps in a rating scale. He said, "more than seven yields an increase in reliability that is hardly worth the trouble."[11] E. S. Conklin, however, concluded on the basis of an analysis of 23,000 judgments, that the maximum number of steps in a scale designed to rate a behavioral quality is five.[12] J. P. Guilford suggested that the number of points on a given rating scale should depend on the motivation and abilities of the observers, and these qualities should be screened before the actual judgments begin.[13] Joseph Wepman used a seven point scale in judging esophageal speech and believes it was too definitive

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[11] P. M. Symonds, "On the Loss of Reliability in Ratings Due to Coarseness of the Scale," J. Exper. Psychol., VII (1924), 460.

[12] E. S. Conklin, "The Scale of Values Method for Studies in Genetic Psychology," Univ. Ore. Pub., II (1923), 2.

[13] J. P. Guilford, Psychometric Methods (New York: McGraw-Hill Book Co., Inc., 1936), 263-79.

and demanding for his purpose.[14] George Shames used a five point scale in his investigation of prognostic evaluations in speech therapy, and found that this size scale was satisfactory.[15]

Before the members of the panel began rating the fluency of actual subjects, they had reached a coefficient of correlation during training sessions of .94.

The panel of judges observed the subjects an average of one time every alternate week of the experimental periods. On the weeks that the subjects were not observed by the panel, two judges (the investigator and one judge) observed the subjects in the children's home environment. It was felt that the reliability of the panel was sufficient to permit the two judges to become a reasonable extension of the panel. The panel was uninformed regarding the dosage being administered to a given subject; nor were they told which subjects were experimental and which were control.

During the regular panel sessions the following procedure was used:

1. The judges were seated in two rows on the observer's side of a one-way vision glass. They were requested to rate the five minute speech sample of each child according to the five point scale, and record their ratings on a form provided.[16] The panel members were also

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[14] Joseph M. Wepman, "The Objective Measurement of Progressive Esophageal Speech Development," The Journal of Speech and Hearing Disorders, XVIII (September, 1953), 247.

[15] George Shames, "An Investigation of Prognosis and Evaluation in Speech Therapy," J. S. H. D., XVII (December, 1952), 387.

[16] Appendix C.

requested to count the number of hesitations, repetitions, or prolongations they heard and to record this number on their rating form. These non-fluency counts were not used for determining change of speech fluency. The counting was requested because the process of counting non-fluencies seemed to help the judges achieve a more objective rating of each subject's speech.

2. The investigator brought a subject into a room on the reflection side of the one-way vision glass. They were seated with the child facing the front of the mirror, and the investigator diagonally across a table from him with his profile to the mirror. The child was told, "I will show you a picture, and you make up a story about it. Tell me a story about this picture." The subject was then shown a picture from the Children's Apperception Test.[17] These pictures were presented in the following order:

first — No. 1

second — No. 10

third — No. 7

fourth — No. 8

fifth — No. 2

sixth — No. 3

seventh — No. 4

eighth — No. 5

ninth — No. 6

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[17]Leopold Bellak and Sonya Bellak, Children's Apperception Test (New York: C. P. S. Co., 1952).

tenth — No. 9

This method seemed to obtain a relatively spontaneous sample of connected discourse without the handicap of the adaptation effect. The investigator, in general, made two types of verbal response to the subjects' statements. He made comments which were essentially neutral, such as, "Oh," "Is that so?", "I suppose," "I see," etc. When a five minute sample of speech had not been obtained, another picture was presented and the performance repeated. If a five minute speech sample still had not been obtained, the investigator asked the subject direct questions such as, "If you could play any game you wanted to, what would you play?", "How do you play that?", "What do you want to be when you get big?", "What does a _____ do that you'd like to do?" Following a five minute sample of speech the subject was given a toy balloon and a lollypop and was returned to his parent.

In order to ascertain a possible relationship between changes in speech fluency and changes of thiamine status, three twenty-four hour urine samples were obtained for the purpose of thiamine assay. These results were then compared to the amount of each subject's thiamine intake which was determined by means of a dietary history.[18] The following schedule was maintained:

1. For one week the mother of each subject completed a dietary history. No tablets were administered during this week.

2. At the end of this first week, a twenty-four hour urine sample was obtained and refrigerated after a preservative, Toluene, was

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[18]Appendix D.

added.

3. The dietary survey was continued throughout the experimental period. After the first week, the subject received either 25 mg. of thiamine or a placebo, three times daily, for a period of not more than five and not less than four weeks.

4. At the end of this first experimental period, another twenty-four hour urine sample was obtained.

5. The subjects who had been receiving thiamine were then administered placebo and vice versa. The dietary history was maintained during this second experimental period.

6. At the termination of the second experimental period, a third twenty-four hour urine sample was obtained.

Prior to the onset of the investigation, a brief pilot study was conducted in an effort to test the efficacy of the method used to determine thiamine level. Twenty adults, ten who stutter, and ten who purportedly do not stutter, were included in the pilot study. Each subject maintained a dietary history for three weeks and ingested 22.4 mg. of thiamine three times daily during the second and third week. Two twenty-four hour urine samples were obtained, one at the end of the first week, and one at the end of the third week.

A modification of the thiochrome method of thiamine assay was used in both the pilot study and the actual investigation.[19] The modification is described by O. Mickelsen as follows:

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[19]The Association of Vitamin Chemists, Inc., Methods of Vitamin Assay (New York: Interscience Pub., Inc., 1947).

In work with urine it has been shown that much if not all of the substances interfering with true blank readings can be eliminated by adding 0.50 to 0.55 ml. of a mixture of equal parts of concentrated HCl. and 85 per cent of H_3PO_4 to the reaction vessels containing the assay solution and the blank solution before shaking with isobutyl alcohol. This brings the pH within the range of 8 to 9.5 where a white precipitate appears. Under these conditions, this thiochrome may be completely extracted from aqueous solution with isobutyl alcohol, but nonthiamine fluorescent substances are largely eliminated.

Methods Used in Analyzing the Results

In as much as the purpose of this research was to study the effects of thiamine on children with speech non-fluency, several comparisons were made between the non-fluent experimental and the fluent control groups, and several relationships between thiamine status and speech fluency status were tested. The following points were analyzed in order to establish results:

1. The subjects' fluency, as rated by the panel of judges, was studied prior to the administration of thiamine or placebo, during both the thiamine and placebo doses, and then the three ratings were compared.

2. The levels of thiamine in the urine of experimental subjects were compared with the thiamine levels of control subjects before the administration of either dose.

3. The thiamine levels of experimental subjects were compared with those of the control subjects after the administration of thiamine.

4. Tests were made of the possible relationship between thiamine levels of the urine and speech fluency.

5. A study was made of the possible relationship between the change in thiamine levels (from the pre-dose to the thiamine dose

samples) and fluency ratings.

6. A comparison was made of the experimental group and the control group's intake of thiamine (as determined by the dietary record report) before either dose was administered.

7. In view of the usually inverse relationship between thiamine and carbohydrate mentioned in the first chapter, a comparison was made of the experimental group's ingestion of carbohydrate and the control group's ingestion of carbohydrate.

8. The relationship between thiamine intake and carbohydrate intake was determined.

9. The fact that the administration of the doses was reversed, made it advisable to compare the level of thiamine in the urine of those subjects taking thiamine first with those taking it as their second dosage.

10. The intake of thiamine through the usual daily diet was compared in subjects who received the thiamine first and those who received the placebo first.

CHAPTER III

PRESENTATION AND EVALUATION OF THE DATA

The results of the study are reported in light of the data obtained through the rating panel's judgments, laboratory determinations of urine thiamine levels, and dietary reports of thiamine and carbohydrate intake. The findings presented here were drawn from the myriad of raw data obtained throughout the course of the study. This raw data is available to the reader in the form of a composite of reportable data.[1]

Before indicating the findings of this investigation, it would seem wise to discuss briefly some of the difficulties encountered during the course of the study. The evaluation of the data must be qualified on the basis of several uncontrollable variables.

Difficulties Encountered

1. The problem of obtaining subjects was emphatically and constantly present throughout the study. This was not surprising in view of the inconveniences required of the subjects and parents involved. At any rate, in an effort to obtain sufficient numbers of subjects, the investigator was forced to decrease the number of visits each subject made to the speech rating panel. Further, the gradual

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[1] Appendix E.

increase in the number of subjects as the study progressed caused subjects to begin their participation at different times. As a consequence, subjects who began the experiment in January may have been compared with subjects who began in March. The reasonable hesitation on the part of some parents to have their children participate also caused the experimental period to be held to a minimum. This may not have hindered the laboratory aspect of the study, but it probably prevented the speech rating panel from obtaining a sufficient number of speech samples during the thiamine and placebo doses.

2. It was impossible to control several factors involved in the study. The investigator is left to assume that each subject ingested three tablets per day as directed. It must also be assumed that the parents involved reported the dietary intake accurately, and equally important, did not increase the child's food intake, quantitatively or qualititatively, once they began participating. The further assumption must be made that each urine sample collected was a continuous, twenty-four hour sample. It is difficult to estimate the accuracy of such assumptions.

3. At the outset of the study it was anticipated that a consistent panel of trained judges would rate each subject during each of the subject's consecutive visits. Although the cooperation of the panel was maximum, it was nevertheless humanly impossible for several of the panel members to be present during every rating session. Therefore, the panel's judgments were not amenable to such reflective measures as correlations of coefficients or analysis of variance. It

was for this reason that the mean ratings of the panel for each subject, on each occasion was used as an indication of agreement. This would seem to be justified because in this case the mean is not distorted by the extremes of the judgments. Essentially, the mean rating represents the panel's rating for a given session.

4. It was hoped that a clear reflection of the thiamine status of subjects would be derived from computing the percentage of thiamine excretion (which in turn is a reflection of the amount ingested and the volume of thiamine in the urine per day). However, the percentage figures did not illustrate increase in thiamine concentration in the urine. The number of micrograms of thiamine per ml. was revealed to be five to nine times as great after the thiamine dose, but the dose was essentially seventy-five times as great as the usual thiamine intake. This tremendous increase was not revealed by studying the volume of urine and the per cent of thiamine within that volume. P. C. Leong had similar findings in experiments with rats and concluded that insufficient urinary excretion of the saturated thiamine dose was caused by the fact that the body fluids were not sufficient to permit urinary excretion of the massive dose. A considerable amount of such a dose may have been eliminated through feces and perspiration.[2] In view of this difficulty, it was decided that a consideration of the concentration of thiamine per ml. of urine would more adequately reflect thiamine status than the volume of urine and its quantity of

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[2] P. C. Leong, "Vitamin B_1 in the Animal Organism: A Quantitative Study of the Metabolism of B_1 in Rats," Biochem. J., XXXI (1937), 373.

micrograms per ml.

Findings

1. According to the rating panel's judgments, there was not a significant difference in the fluency of subjects who were administered thiamine and those who were given placebo.

A comparison of speech ratings during the pre-dose speech screening, the thiamine doses, and the placebo doses can be seen in Table I, on the next page. A slight, gradual improvement in fluency was made during the progress of the investigation, but this may be a reflection of the fact that only subjects who were judged as 2.00 or higher on the scale during the pre-dose screening were designated as experimental subjects. As the study continued, some judgments of less than 2.00 were likely to accrue. Regardless of this tendency of the subjects to show slight improvement throughout the course of the study, it is clear that as much increase in fluency occurred during the placebo dose as occurred during the thiamine dose.

2. There was not a significant difference in the concentration of thiamine in the urine samples of the experimental subjects and the urine samples of control subjects before the administration of thiamine.

Experimental Subjects:	M = .142 γ per ml.	SD = .20
Control Subjects:	M = .100 γ per ml.	SD = .14

It was clearly indicated by the presence of thiamine in the urine that neither group was thiamine deficient to begin with. Apparently the subjects of both groups did not suffer from any metabolic "lesions" which might have prevented their thiamine intake from being

TABLE I

JUDGMENTS OF NON-FLUENCY UNDER THIAMINE AND PLACEBO DOSES

Assigned Values	Judges Ratings	Pre-dose Screening	Placebo Occasion 1	Placebo Occasion 2	Thiamine Occasion 1	Thiamine Occasion 2
15	3.81-4.00	2	1		2	1
14	3.61-3.80	1	1		0	0
13	3.41-3.60	0	0		0	0
12	3.21-3.40	2	0	1	0	0
11	3.01-3.20	2	2	1	4	0
10	2.81-3.00	5	5	4	6	3
9	2.61-2.80	3	1	0	0	1
8	2.41-2.60	0	1	0	0	0
7	2.21-2.40	1	1	0	0	0
6	2.01-2.20	5	3	2	3	0
5	1.81-2.00	8	11	4	9	4
4	1.61-1.80		1	0	1	0
3	1.41-1.60			0	0	0
2	1.21-1.40			0	0	0
1	1.01-1.20			2	0	1
0	.81-1.0		2		4	3
Number:		29	29	14	29	13
Mean:		8.41	6.97	6.93	6.93	5.77
SD:		3.35	3.46	3.45	4.11	5.01
SDm:		0.63	0.65	0.96	0.78	1.45

properly assimilated and utilized.

3. The relationship of the urine thiamine level and speech ratings (before the administration of thiamine), was not significant as revealed by means of the Pearson product-moment coefficient of correlation.

$r = +\ 0.3$ Not significant at the 5% level of confidence.

This appears to indicate a slight tendency, probably within the realm of chance, that the greater the concentration of thiamine in the urine, the greater the non-fluency. If thiamine were to have been considered as having a direct and beneficial effect upon non-fluency, it would have been reasonable to assume that when the non-fluency had been judged as relatively severe, there would have been an accompanying condition of relatively low thiamine level. According to the findings of this investigation, there was no relationship between low thiamine levels and high degree of non-fluency. The circumstance of higher thiamine levels accompanying more severe non-fluency did not occur consistently enough to be considered significant, and may, in part, be explained by the fact that the non-fluent group was larger and therefore had greater variations in thiamine levels than did the fluent group.

4. The relationship of the urine thiamine level and speech ratings after the administration of thiamine was revealed as not being significant.

$$r = + 0.032$$

This finding would seem to indicate that saturated doses of thiamine did not serve to change the non-fluency pattern in either

direction. Increase in thiamine level did not manifest itself in subsequent and consistent decrease in non-fluency.

5. The relationship of the change in thiamine levels (after the administration of thiamine) and fluency ratings did not appear to be significant.

$$r = + 0.045$$

This consideration of the amount of change in the concentration of thiamine which occurred after the increased dosage, indicated that the subjects in whom this change was greatest had no accompanying change in non-fluency. For that matter, those subjects who revealed little change in thiamine levels after the thiamine dose showed no significant change in non-fluency.

6. A comparison of the pre-dose intake of thiamine in the experimental group and the control group revealed that the experimental subjects had a significantly higher intake of thiamine.

Experimental Subjects: M = 2.124 mg.
Control Subjects: M = 0.984 mg.

This finding was, in part, reflected in finding number 2, in that the experimental group's greater thiamine intake would seem to account for the greater concentration of thiamine in the urine. The fact that the non-fluent group consumed more thiamine in their diets than the fluent group, (despite the fact that neither group was thiamine deficient), may be explained in view of the greater variations occurring within the non-fluent group. It is reasonable to assume that the larger the group, the greater will be the variation among the subjects within that group. Then too, dietary thiamine intake is a

difficult factor to evaluate properly because small and temporary dietary changes from day to day and from meal to meal may be revealed clearly in the average daily thiamine intake and consequently are weighted heavily in comparisons of the average of B_1 intake of the two groups.

7. A comparison of the experimental and control groups' intake of dietary thiamine during the thiamine dosage, revealed that the experimental group tended to have a higher intake of thiamine.

Experimental Subjects: M = 76.333
Control Subjects: M = 75.966

This appeared to be a significant difference at the one per cent level of confidence. The greater number of subjects in the experimental group permitted a larger variability between subjects and this may, in part, account for the difference between the two groups.

8. The subjects who were given thiamine as the first dose as compared with subjects who received thiamine as the second dose were not significantly different in the quantity of micrograms per ml. of urine they excreted.

Thiamine First: M = 0.378 micrograms per ml.
Thiamine Second: M = 0.412 micrograms per ml.

If the subjects who received thiamine as their first dose had shown improvement and then continued this improvement during the placebo period, it might have been assumed that the beneficial effect of thiamine was being carried over into the placebo period. However, the fact that those subjects who received placebo first showed as much improvement as those who received placebo after taking thiamine, would tend to negate any assumption that thiamine had a beneficial effect that was

continued after the cessation of the vitamin dose.

9. A comparison of the micrograms per ml. or urine of the experimental and control groups, following the administration of thiamine, revealed no significant difference between the two groups.

Experimental Subjects: M = .392 micrograms per ml.
Control Subjects: M = .347 micrograms per ml.

This finding is not surprising in view of finding number 2, which indicated there were no differences between the two groups in thiamine concentration before the thiamine dose. Taken together, the two findings rather definitely preclude any differences between the two groups in regard to the need for, or use of thiamine.

10. The subjects administered thiamine as the first dose, as compared with those who were given thiamine as the second dose, were not significantly different in their intake of thiamine through their regular diet.

Thiamine First: M = 76.829 mg.
Thiamine Second: M = 76.594 mg.

It was apparent that the administration of concentrated doses of thiamine did not cause the subjects to increase their ingestion of foods which contained thiamine.

11. A comparison of the pre-dose urine sample and the placebo dose urine sample, revealed no significant differences in the volume of thiamine per ml. of urine.

Pre-dose: M = .142 micrograms per ml.
Placebo dose: M = .191 micrograms per ml.

It was clear that an increased thiamine concentration in the urine was not maintained for any appreciable length of time. This

appears to agree with previous studies of thiamine-urine levels before and after thiamine intake.

12. The relationship of the intake of thiamine through ingestion of food and the speech ratings (before the administration of thiamine) was not significant.

$$r = + 0.07$$

This was reflected in finding number 3, and both findings tended to exclude the existence of a relationship, inverse or direct, between thiamine ingestion and judgments of speech fluency.

13. There appeared to be some indication that the administration of thiamine is related to an increase in carbohydrate intake, but this indication did not seem to be statistically convincing in view of the small number of subjects involved.

Carbohydrate during Pre-dose Dietary Survey: M = 158.25 g
Carbohydrate during Thiamine Administration: M = 170.14 g
Carbohydrate during Placebo Administration: M = 159.36 g

For the subjects studied there is a probability of eighty-five chances out of one hundred that thiamine caused an increase in carbohydrate intake.

Although finding number 10 revealed that thiamine dosage did not cause subsequent increase in dietary thiamine intake, finding number 13 seemed to indicate that if thiamine caused an increase in appetite, it was reflected in greater ingestion of carbohydrate as might be expected from previous studies of the effect of thiamine on the appetite and subsequent increase in various nutrients.

14. There seemed to be a negative correlation between carbohydrate intake before the dose and the degree of non-fluency.

$r = -0.509$ Significant at the 1% level of confidence.

In general, then, there is an indication that the higher the intake of carbohydrate on the pre-dose dietary survey, the greater the fluency.

This relationship might have been consistent enough to be considered causal; however, the following seven findings served to negate the significance of this relationship between high carbohydrate intake and the severity of non-fluency. The fact that such a definite relationship was revealed in the first place may be attributed to the difficulty involved in quantitative consideration of carbohydrate intake. As stated earlier, carbohydrate intake varies greatly from day to day and meal to meal, (not only for a given group, but individually as well). Comparisons of carbohydrate daily averages frequently reflect temporary extremes of either high or low carbohydrate ingestion. In view of this fact, together with a consideration of the seven findings which follow, it was believed that a predictable relationship between high carbohydrate intake did not exist.

15. The relationship of carbohydrate intake and fluency during the administration of thiamine, was not significant.

16. When the carbohydrate intake of subjects who were administered thiamine for the first dose were compared with the carbohydrate intake of subjects who were given thiamine for the second dose, no significant difference was discovered.

Carbohydrate Intake, thiamine dose first: $M = 165.49$ g.
Carbohydrate Intake, thiamine dose second: $M = 163.42$ g.

17. The correlation between carbohydrate intake and judged degrees of non-fluency during the placebo dose was not significant.

$$r = + 0.176$$

18. A comparison of the carbohydrate intake of the experimental and control groups before the administration of either dose revealed a difference which was barely significant.

Experimental Subjects:	M = 158.25 g	SD = 23.03
Control Subjects:	M = 140.17 g	SD = 36.07

$$t = 2.07$$

This finding provided significant evidence which pointed to the inconsistency of finding number 14. If greater carbohydrate intake were related to greater fluency, it would be logical to assume that the fluent control subjects would have had higher carbohydrate intakes than the non-fluent experimental groups. Finding number 18 revealed the inaccuracy of such an assumption.

19. A comparison of the carbohydrate intake of the experimental and control groups during the thiamine dose revealed no significant difference between the two groups.

$$t = 1.69$$

20. The negative correlation between the carbohydrate intake (before the administration of either dose) and the quantity of thiamine per ml. of urine (before either dose) did not appear to be significant.

$$r = -.136$$

21. The negative correlation between carbohydrate intake and the quantity of thiamine per ml. of urine (during the administration of thiamine) was apparently not significant.

$$r = -.145$$

22. A comparison of ten adult male stutterers with ten adult

non-stutterers, revealed essentially no differences between the two groups in regard to total urine excretion, thiamine levels before the dose, and thiamine levels after the dose. There were virtually no differences between the two groups as far as dietary intake is concerned. There appeared to be a greater range of variability among the stuttering group, but this probably is explained by the fact that the stuttering group was largely comprised of students at the University of Florida and their ingestion of both liquids and solids proved to be irregular and unpredictable.

CHAPTER IV

SUMMARY AND CONCLUSIONS

Assuming that the panel's rating of speech on a five point scale provided an accurate measure of non-fluency, and assuming that laboratory analyses and dietary histories provided reliable pictures of nutritional status, several conclusions were reached.

Conclusions

1. There appeared to be no consistent, significant differences between those subjects judged as non-fluent and those judged as fluent.

2. In general, there appeared to be no justification for stating that thiamine had an observably favorable effect upon speech non-fluency of the subjects involved.

3. There appeared to be no justification for stating that thiamine had an observably unfavorable effect upon the speech non-fluency of the subjects involved.

4. The results of this investigation would seem to indicate that there was some additional support for the previous studies which have found no physical differences between those individuals who stutter or are non-fluent and those who are relatively fluent.

In view of such factors as the small number of non-fluent children uncovered during the study, the many divergent viewpoints

regarding the nature of non-fluency which were manifested within the rating panel when it first assembled, and the existence of apparently different types of non-fluency, the following recommendations for separate or conjoint research were made.

Recommendations

1. A study of the incidence of non-fluency should be conducted, and should consider factors such as the socio-economic level of parents, endemic and cultural characteristics of the family, numbers of siblings, and environmental permissiveness regarding speech.

2. An investigation of the validity and reliability of judgments of non-fluency should be made, and ought to include ratings by trained and untrained judges.

3. A study of the nature of non-fluency should be conducted, and should include consideration of different types of non-fluency, comparisons of degrees of muscular tension during non-fluent utterance, and a search for a possible transitional stage between non-fluency which is normal and that which should be regarded as pathological (secondary stuttering).

APPENDIX A

SPEECH SURVEY AND RELATED RESEARCH
DEPARTMENT OF SPEECH
SPEECH AND HEARING CLINIC
UNIVERSITY OF FLORIDA

_____
Date

Dear

I would like to take this opportunity to thank you for your participation in our research project. The cooperation we have received has been very encouraging, and we certainly appreciate the important help you have given us. In many instances we have not sent out these reports as promptly as we would have liked, but we hope you will understand the many problems which arise when dealing with large numbers of individuals in a limited period of time and with moderate resources.

That which follows is a brief report on the aspect of our study in which your child participated. It consists of a description of how your child appeared to perform according to the judgments of our seven qualified panel members.

Child's Name_____

General Speech Survey_____

_____

_____

Articulation_____

_____

_____

Voice_____

_____

Other factors_____

_____

_____

Recommendations_____

_____

_____

_____

Thank you again for your kindness and cooperation. We will be glad to try to answer any questions you might have concerning this study, and if we can serve you in any way please let us know.

Sincerely yours,

Edward M. Penson

APPENDIX B

March 3, 1955

Mr. Edward M. Penson is doing some research for his doctor's degree at the University of Florida which requires the administration of certain tablets to the children who are being used as subjects for his controlled study. These tablets have been made up and given to this research project by a pharmaceutical firm and are entirely nutritional in nature and could not, under any circumstances, be considered harmful. I have been in close contact with Mr. Penson in the development and conduct of this study and am thoroughly aware of the contents of these tablets and the instructions for their use. While it would not be necessary to obtain medical prescription in order to purchase similar tablets from a drug store, in order to give medical approval of this procedure you may regard this letter as my prescription for their use in connection with Mr. Penson's research.

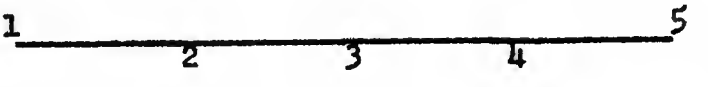
Raymond S. Camp, M.D.

APPENDIX C

Judges Name or Number _____

Subject Number _____

Date _____



Please circle a point on the scale according to your judgment of the degree of non-fluency for this individual.

APPENDIX D

	BREAKFAST	SNACK	LUNCH	SNACK	SUPPER	SNACK
SUNDAY						
MONDAY						
TUESDAY						
WEDNESDAY						

	BREAKFAST	SNACK	LUNCH	SNACK	SUPPER	SNACK
THURSDAY						
FRIDAY						
SATURDAY						

APPENDIX E

COMPOSITE OF DATA

Subject	Dose	Vol. of Urine/ ml.	B_1 γ/ml.	B_1 γ/day	B_1 Intake mg.	Carbohydrate Intake g.	Mean Fluency	% B_1 Excreted
21	pre/	560	0.346	193.8	2.475	126.4	3.75	7.83
21	B_1	530	1.28	679.06	75.72	98.92	3.0	0.90
21	x	880	0.144	127.5	.746	127.4	2.0	17.09
21A*	pre	550	0.012	6.68	2.18	150.56	1.0	0.31
21A	B_1	550	0.102	56.10	77.32	175.267	1.0	0.07
21A	x	380	0.172	65.31	2.285	192.05	1.0	2.86
22	pre	820	0.34	276.75	6.75	166.843	2.78	4.10
22	B_1	500	0.019	9.80	82.423	166.467	1.78	0.01
22	x	740	0.135	99.26	4.61	153.92	2.22	2.15
23	pre	845	0.065	55.06	1.67	170.25	2.88	3.30
23	x	780	0.015	11.51	1.79	127.65	2.11	0.64
23	B_1	540	0.26	140.9	76.102	163.343	1.0	0.19
23A	pre	550	0.33	183.33	1.03	132.55	1.0	17.71
23A	x	830	0.028	23.24	5.58	153.1	1.0	0.42
23A	B_1	680	0.615	418.20	76.47	163.833	1.0	0.55
24	pre	550	0.015	9.4	.96	145.9	2.11	0.88
24	x	430	0.019	8.14	.99	140.67	1.82	0.82
24	B_1	580	0.45	262.74	76.293	145.47	1.0	0.34
25	pre	480	0.096	46.53	2.04	191.0	2.0	2.28
25	x	420	0.43	183.07	1.80	184.95	3.18	10.17
25	B_1	470	0.415	195.05	76.92	211.933	2.14	0.25
25A	pre	440	0.057	25.52	.573	67.325	1.0	4.45
25A	B_1	300	0.423	126.9	75.29	55.085	1.0	0.17
26	pre	450	0.173	78.06	2.06	128.843	3.0	3.78
26	B_1	470	1.123	527.81	76.66	165.6	3.20	0.69
26	x	580	0.82	48.03	1.62	142.825	3.88	2.96
26A	pre	580	0.493	286.52	.808	186.123	1.0	33.23
26A	B_1	470	0.317	148.99	75.56	147.41	1.0	0.20
27	pre	550	0.071	39.29	.56	171.033	2.38	7.02

* = A = Control subject (fluent)
/ pre = Before either dose
x = Placebo dose

Subject	Dose	Vol. of Urine/ ml.	B_1 γ/ml.	B_1 γ/day	B_1 Intake mg.	Carbo-hydrate Intake g.	Mean Fluency	% B_1 Excreted
27	B_1	470	0.219	102.93	78.837	187.733	3.10	0.13
27	x	320	0.006	1.95	.943	165.1	1.89	0.21
27A	pre	660	0.022	15.18	.553	68.20	1.0	2.75
27A	B_1	270	0.625	171.450	75.51	126.833	1.0	0.23
28	pre	1850	0.081	151.02	2.014	148.805	3.22	4.5
28	x	1100	0.13	143.0	2.128	153.2	3.09	6.72
28	B_1	1600	1.029	1646.4	76.596	169.627	2.11	2.15
28A	pre	750	0.076	57.08	.83	170.93	1.0	6.88
28A	B_1	380	0.088	33.44	75.853	209.933	1.0	0.04
29	pre	320	0.025	8.0	1.546	173.733	2.11	0.52
29	B_1	620	0.40	248.0	76.18	153.233	2.09	0.33
29	x	280	0.084	23.8	3.39	160.643	2.0	0.70
30	pre	250	0.044	11.17	.83	186.04	2.00	1.35
30	x	590	0.024	1.273	1.27	167.643	2.11	0.10
30	B_1	590	0.548	323.32	76.51	90.5	2.0	0.42
31	pre	235	0.203	47.94	1.99	153.33	3.10	2.41
31	B_1	360	0.185	66.60	76.083	199.933	2.89	0.09
31	x	190	0.057	14.44	.58	123.167	2.56	2.49
31A	pre	420	0.029	12.18	.76	180.233	1.0	1.59
31A	B_1	460	0.308	141.22	75.723	129.525	1.0	0.19
31A	x	320	0.077	24.64	.673	175.8	1.0	3.66
32	pre	470	0.013	6.03	.56	153.3	2.00	1.08
32	B_1	470	0.022	10.16	76.453	150.467	2.0	0.01
32	x	190	0.685	130.15	.57	101.443	2.0	22.83
33	pre	420	0.153	64.29	1.46	191.682	2.0	4.40
33	B_1	350	0.174	60.90	76.958	201.467	1.00	0.08
33	x	280	0.607	169.96	.58	112.277	1.0	29.30
33A	pre	580	0.046	26.68	.78	150.233	1.0	3.42
33A	B_1	875	0.342	299.25	76.01	211.967	1.0	29.63
34	pre	430	0.082	35.10	6.12	174.0	2.18	0.57
34	x	1340	0.014	18.61	.7	227.65	1.78	2.66
34	B_1	780	0.046	35.88	77.27	180.24	3.86	0.05
34A	pre	230	0.034	7.83	.89	166.329	1.0	0.88
34A	x	465	0.069	32.08	.981	175.1	1.0	3.27
34A	B_1	230	0.026	5.98	75.98	166.05	1.0	0.008
35	pre	260	1.137	295.75	1.72	160.75	2.18	17.16
35	x	520	0.042	21.84	2.16	185.7	2.67	1.01
35	B_1	250	0.175	43.75	77.738	158.256	2.0	0.06

* = A = Control subject (fluent)
pre = Before either dose
x = Placebo dose

Subject	Dose	Vol. of Urine/ ml.	B_1 γ/ml.	B_1 γ/day	B_1 Intake mg.	Carbo-hydrate Intake g.	Mean Fluency	% B_1 Excreted
35A	pre	680	0.527	358.36	1.7	136.85	1.0	21.08
35A	B_1	560	0.638	357.28	77.134	265.033	1.0	0.46
36	pre	740	0.061	44.87	2.02	150.353	2.18	2.22
36	x	780	2.101	163.883	1.583	183.393	2.00	10.35
36	B_1	680	1.20	816.0	76.643	142.286	2.00	1.06
37	pre	550	0.244	133.974	1.98	159.533	3.18	6.77
37	B_1	680	0.846	57.538	77.576	279.933	3.11	0.07
37	x	580	0.123	71.34	2.32	180.71	1.88	3.08
37A	pre	440	0.019	8.657	.?	106.167	1.0	1.24
37A	B_1	385	0.742	285.67	75.76	114.54	1.0	0.38
38	pre	590	0.013	8.194	1.16	136.2	3.82	0.70
38	B_1	700	0.461	323.4	77.92	305.10	3.89	0.42
38	x	770	0.088	67.941	2.64	192.1	3.0	2.57
38A	pre	630	0.057	36.54	.993	140.6	1.0	3.68
38A	B_1	690	0.161	111.78	76.2	171.925	1.0	0.15
39	pre	440	0.115	50.769	.743	148.267	2.0	6.83
39	B_1	300	0.615	184.5	75.66	138.30	1.0	0.24
39	x	190	0.028	14.55	1.05	146.77	1.0	1.39
39A	pre	730	0.012	8.76	.686	122.966	1.0	1.28
39A	B_1	430	0.228	98.04	75.72	111.54	1.0	0.13
39A	x	170	0.72	12.218	.745	93.29	1.0	1.64
40	pre	820	0.015	12.74	6.46	227.9	2.0	0.20
40	x	450	0.021	9.45	.98	209.23	1.88	0.96
40	B_1	370	0.307	113.96	79.2	231.73	2.0	0.14
41	pre	540	0.04	21.75	1.36	128.7	2.82	1.60
41	B_1	380	0.403	15.34	75.48	112.13	2.89	0.02
41	x	430	0.042	18.06	.827	213.5	3.0	2.18
41A	pre	510	0.03	15.3	.58	157.03	1.0	2.64
41A	B_1	310	0.317	98.27	75.78	150.03	1.0	0.13
42	pre	240	0.019	4.5	7.42	166.47	3.22	0.06
42	B_1	260	0.053	13.78	75.83	185.91	3.14	0.02
42	x	320	0.097	30.74	5.48	160.51	2.0	0.58
42A	pre	440	0.067	29.63	1.08	189.07	1.0	2.74
42A	B_1	310	0.55	169.26	75.86	181.57	1.0	0.22
42A	x	340	0.013	4.43	.84	202.8	1.0	0.53
43	pre	900	0.038	34.33	.697	153.33	2.0	4.93
43	B_1	1140	0.103	118.56	75.74	185.8	2.0	0.16
43	x	820	0.035	28.7	.87	209.63	2.0	3.30

* = A = Control subject (fluent)
≠ pre = Before either dose
x = Placebo dose

Subject	Dose	Vol. of Urine/ ml.	B_1 γ/ml.	B_1 γ/day	B_1 Intake mg.	Carbo-hydrate Intake g.	Mean Fluency	% B_1 Excreted
43A	pre	240	0.11	26.62	1.96	201.47	1.0	1.36
43A	B_1	430	0.377	162.11	76.63	124.53	1.0	0.21
43A	x	340	0.023	7.82	.925	77.4	1.0	0.85
44	pre	450	0.27	121.15	.627	160.35	2.78	19.32
44	x	290	0.042	12.18	.563	132.1	2.0	2.16
44	B_1	570	0.37	212.61	75.58	194.86	2.0	0.28
44A	pre	260	0.042	10.92	.768	161.7	1.0	1.42
44A	B_1	170	0.053	9.01	75.69	105.27	1.0	0.01
44A	x	140	0.05	7.0	.628	132.37	1.0	1.11
45	pre	450	0.19	89.42	2.93	137.57	2.89	3.05
45	x	590	0.05	31.86	.507	101.63	2.12	6.28
45	B_1	750	0.46	346.5	75.74	124.1	2.0	0.46
46	pre	60	0.075	4.54	1.306	151.46	2.0	0.36
46	B_1	80	0.104	8.32	76.94	153.52	2.0	0.01
46	x	70	0.08	5.53	1.91	152.93	2.0	0.29
46A	pre	500	0.01	59.12	1.39	127.28	1.0	4.25
46A	B_1	430	0.105	45.58	75.67	101.6	1.0	0.06
46A	x	410	0.12	50.43	.7	125.97	1.0	7.2
47	pre	490	0.23	114.2	.57	139.07	4.0	20.0
47	x	400	0.092	36.8	.817	182.06	3.0	4.5
47	B_1	300	0.02	6.3	75.68	177.6	3.0	0.008
47A	pre	420	0.117	49.56	.926	140.72	1.0	5.35
47A	B_1	670	0.7	470.34	75.53	90.70	1.0	0.62
48	pre	590	0.04	24.78	.458	143.84	3.77	5.41
48	B_1	130	0.02	2.26	75.49	181.23		0.003
48A	pre	170	0.068	11.6	.58	95.63	1.0	2.0
49	pre	400	0.017	6.94	2.16	131.63	2.88	0.32
49	x	100	0.06	6.2	.72	137.07	3.0	0.86
49	B_1	80	0.056	4.64	75.434	138.3	3.0	0.006
49A	pre	510	0.04	2.25	.72	170.27	1.0	0.31
49A	B_1	230	0.2	48.07	75.63	137.0	1.0	0.06
50	pre	330	0.2	67.32	.993	192.37	2.67	6.78
50	B_1	220	0.16	36.3	75.88	155.93	2.88	0.05
50A	pre	650	0.04	24.7	1.58	107.03	1.0	1.56
50A	B_1	600	0.37	221.4	75.94	185.87	1.0	0.29
51	pre	790	0.09	69.52	.67	127.73	3.0	10.05
51	B_1	710	0.37	262.7	75.69	154.67	3.0	0.35
52	pre	250	0.035	18.36	3.62	182.43	3.14	0.51
52	B_1	240	0.62	150.0	78.2	165.05	3.8	0.19

* = A = Control subject (fluent)
ǂ pre = Before either dose
x = Placebo dose

APPENDIX F

INVESTIGATOR'S SUBJECTIVE DESCRIPTION OF SUBJECTS' NON-FLUENCY

Subject: 21, Age: 5, Sex: Male

This subject's non-fluency seemed to be characterized by both repetition of syllables and prolongation of sounds in the initial position. The frequency and severity of the non-fluency did not appear to vary significantly from the first observation to the last. The quantity of the speech sample obtained during observation sessions was adequate throughout the study. Toward the end of the investigation, the subject seemed to become familiar with the speech sampling procedure and discourse tended to be more freely elicited.

Subject: 22, Age: $4\frac{1}{2}$, Sex: Male

This child's pattern of non-fluency appeared to consist of frequent pauses between phrases and between words within a phrase. There seemed to be some decrease in non-fluency during the final stages of the investigation (during the administration of the placebo dose). This subject appeared to be extremely shy and speech responses were elicited with difficulty. Repeated exposure to the observation sessions did not seem to effect the subject's tendency to be reticent.

Subject: 23, Age: $4\frac{1}{2}$, Sex: Female

Analysis of this individual's non-fluency revealed repetition

of syllables and words. Mild and inconsistent improvement seemed to occur during the last stage of the investigation (during the thiamine dose). The child apparently had little or no hesitancy in regard to expressing herself throughout each observation session. On several occasions she related that she wanted to "talk about those pictures," and during each interview, her discourse was accompanied by considerable facial and vocal animation.

Subject: 24, Age: 4, Sex: Male

By and large, this subject's non-fluency was characterized by short, hyper-tense, but infrequent blocks which occurred at the beginning of some words. There did not appear to be any consistent improvement in fluency during the course of the study. The child verbalized with comparative ease, but rarely followed a given line of thought for any length of time. He appeared to be rather excitable and gave the impression of being easily distracted.

Subject: 25, Age: $3\frac{1}{2}$, Sex: Male

This subject's non-fluency consisted of repetitions of phrases, words, and syllables. Prolongations or blocks were essentially non-existent. The subject was rated by the panel as being more non-fluent during the placebo and vitamin doses than at the time of his pre-dose screening. His non-fluency appeared to become more hypertense as the study progressed. There seemed to be no tendency on the part of the child to withdraw from the interview situation. He cooperated on all occasions and expressed his enjoyment after each session.

Subject: 26, Age: 3, Sex: Male

Analysis of this child's non-fluency revealed a pattern consisting of frequent repetitions of words and occasional blocks on sounds in the initial position. This pattern was similar to the stuttering pattern of the boy's father, who considers himself a "controlled stutterer." There was no marked abatement of the non-fluency during either dose. The subject seemed willing enough to enter the interview session, and considering the age of the child, verbal output was at least adequate.

Subject: 27, Age: 3, Sex: Male

This subject's non-fluency was characterized by frequent repetitions of syllables, words, and phrases. Occasionally the pattern included a relatively hypertense block on sounds in the initial position. There seemed to be a mild decrease in the quantity and severity of the non-fluency as the study continued. This youngster verbalized quite freely, and the interview sessions revealed his apparent propensity for story-telling, teasing, and argument.

Subject: 28, Age: 6, Sex: Male

The non-fluency demonstrated by this child consisted or repetitions of sounds, syllables, and less frequently, words. Other non-fluent patterns were virtually absent. There appeared to be slight improvement during the last weeks of the thiamine dose. This subject began each interview session with a protest against his participation in the study. However, his conversation during the sessions was both voluminous and continuous.

Subject: 29, Age: 4½, Sex: Male

Consideration of this subject's non-fluency suggested a pattern of sound prolongations and occasional blocks on sounds in the initial position. During any given conversation there was considerable variation in the frequency and severity of the non-fluency. There seemed to be some increase in non-fluency toward the end of the thiamine dose and the beginning of the placebo dose. This subject appeared to be rather shy throughout the course of the study, but after the initial interview, speech was elicited with comparative ease.

Subject: 30, Age: 4½, Sex: Male

Prolongations, hesitations, and repetitions were all part of this subject's pattern of non-fluency. Most of these non-fluencies seemed to be uttered without apparent tension and their frequency varied from one moment to the next. The non-fluent symptoms did not seem to change in one direction or the other from the first interview to the last. The child usually attempted to withdraw from the interview situation, and utterance was quantitatively small throughout the study.

Subject: 31, Age: 5, Sex: Female

This subject's non-fluency consisted primarily of blocks and prolongations of sounds in the initial position. On occasion, these non-fluencies were accompanied by varying degrees of observable muscular tension. There did not appear to be any significant or consistent changes in the symptoms from the outset of the investigation until its conclusion. The child did not give the interviewer the impression of being exceptionally shy, and verbal output was adequate during each

interview.

Subject: 32, Age: 3½, Sex: Male

The non-fluency of this subject was characterized by rare, but hyper-tense repetitions of sounds or syllables. The child gave the interviewer the impression that he was unaware of the occurence of the non-fluent pattern. The non-fluency seemed to remain essentially unchanged throughout the investigation. During the interview this youngster did not seem outwardly shy, but it was difficult to stimulate a quantity of utterance in view of the child's apparent fear of making a mistake. Toward the end of the study, the child seemed to modify this fear, and discourse was more easily elicited.

Subject: 33, Age: 5, Sex: Male

Analysis of this subject's non-fluency revealed a pattern which included occasional repetitions of syllables. For the most part the repetitions were uttered in a relatively relaxed manner; however, on rare occasions a given repetition was articulated as much as six times over again, in what appeared to be a clonic spasm. The non-fluent symptoms were in remission after the pre-dose screening session and continued to be that way throughout both doses. The child appeared to be verbally aggressive, and the interview situations did not seem to bother him. An adequate speech sample was obtained during each session with relative ease.

Subject: 34, Age: 5, Sex: Female

The non-fluent pattern of this subject's speech included pauses

between phrases, tonic blocks, and sound prolongations. On occasion there seemed to be a considerable amount of muscular hypertension accompanying each block. The child also had a relatively severe articulation problem. There did not appear to be any significant change in the severity of non-fluency throughout most of the investigation. However, at the last observation period, during the time the child was receiving thiamine, there was a sudden increase in the severity of the non-fluency. At no time during the study was the child lacking in verbal output.

Subject: 35, Age: 5½, Sex: Male

This child's non-fluency was characterized by mild pauses between words and phrases and occasional repetitions of words. The symptoms did not appear to change markedly throughout the course of the study. The youngster tended to be rather reticent, and seemed to be worried about the interview situations. This worry diminished somewhat whenever the child discussed the subject of fishing.

Subject: 36, Age: 6, Sex: Male

Analysis of this child's speech non-fluency revealed sound prolongations and occasional blocks on sounds in the initial position. For the most part, the blocks and prolongations were experienced without apparent hyper-tension. The pattern of fluency did not significantly improve or worsen during the study. The child gave the investigator the impression of being rather shy; and speech responses were difficult to elicit.

Subject: 37, Age: 7, Sex: Female

A study of the pattern of this child's non-fluency revealed frequent repetitions of words and syllables and some infrequent prolongations and blocks on sounds in the initial position. The symptoms did not seem too hypertense, but the rate of speech utterance was extremely rapid. There appeared to be some improvement of the non-fluency during the last week of the vitamin dosage, and, by and large, this improvement was maintained throughout the placebo dose. The child seemed comparatively reluctant to verbalize, but this reluctance seemed to diminish somewhat during the last two interviews.

Subject: 38, Age: 6, Sex: Female

This child's non-fluent symptoms were characterized by a pattern similar to that of her sister, the preceding subject, number 37. There were frequent repetitions of words and syllables, and occasional prolongations and blocks on sounds in the initial position. There appeared to be some speech improvement during the last week of the thiamine dose. This improvement was maintained and slightly increased during the administration of placebo. Unlike her older sister, this subject seemed willing to converse at almost any and all times.

Subject: 39, Age: 6, Sex: Female

Analysis of this subject's non-fluency indicated mild repetitions of words. After the second week of the experiment there appeared to be relatively no non-fluency of consequence. The youngster seemed hesitant to enter the interview situation and discourse was obtained

slowly. There was only slight abatement of this hesitancy during the course of the investigation.

Subject: 40, Age: 5, Sex: Male

This subject demonstrated a non-fluent pattern consisting of prolonged, but apparently relaxed pauses between some words. This pattern was essentially unique to this subject. His vocabulary appeared noticeably infantile, and many of his mannerisms and activities seemed immature. The pattern and extent of this child's non-fluency did not change markedly throughout the study. The child's apparent lack of verbal output seemed to be due to lack of thought content and language versatility rather than to shyness or fear of the speaking situation.

Subject: 41, Age: 5, Sex: Female

The pattern of non-fluency evidenced by this subject included repetitions of syllables, words, and phrases. These repetitions sometimes seemed to be accompanied by muscular hypertension. There were no significant and consistent changes in the degree of non-fluency from the beginning to the end of the study. At the outset of each interview situation, the child appeared to be inclined toward shyness. As the session continued, however, speech responses were obtained without difficulty.

Subject: 42, Age: 6, Sex: Male

This subject's non-fluency consisted of blocks and prolongations on sounds in the initial position. With a rather unpredictable frequency these non-fluencies were accompanied by some hypertension

especially around the lips. There seemed to be a slight improvement during the last two weeks of the placebo dosage. The child protested against having to look at pictures before each observation session, but after the first picture was presented, his attitude apparently changed, and he seemed to become engrossed in the interview procedure.

Subject: 43, Age: 5, Sex: Female

The non-fluency of this subject was characterized by pauses between phrases, together with great distractibility. The child began talking about one subject, paused, and then continued discussing another -- and sometimes an apparently unrelated -- topic. There may have been a causal relationship between this pattern of interrupted discourse and the child's customary fear of strangers and unfamiliar situations. There were no changes in the observed speech pattern throughout the entire investigation.

Subject: 44, Age: 5, Sex: Female

This subject demonstrated a non-fluent pattern which included repetitions of syllables and words. The repetitions in and of themselves did not seem to be uttered with great degrees of hypertension, but the rapidity and arhythm of the speech delivery gave one the impression of considerable tension. There were essentially no changes, for better or worse, during the child's participation in the study. After the first few moments of the first interview, there was apparently little or no difficulty involved in obtaining an adequate speech sample.

Subject: 45, Age: 3, Sex: Male

Analysis of this subject's non-fluency indicated that blocks on sounds in the initial position together with occasional prolongations comprised the main patterns. There appeared to be some slight improvement during the last part of the placebo dose, which was maintained during the vitamin administration. The subject demonstrated considerable reluctance to enter the interview situation, but once underway, it was not difficult to elicit speech responses.

Subject: 46, Age: 6, Sex: Male

A study of this child's pattern of non-fluency revealed the presence of mild blocks on and pauses before the first sound of some words. The child apparently had little change occur in his non-fluent pattern during the investigation. It seemed to the investigator that this youngster very decidedly wanted to befriend the interviewer, but was uncertain as to how to go about it. During a given interview he would lean very close to the writer, hold his hand, and then say only a very few words. This procedure was followed during all interview periods.

Subject: 47, Age: 5, Sex: Male

The non-fluency of this subject was characterized by repetitions of syllables. There were no observable blocks or prolongations. There did not appear to be any significant improvement during the course of the study. The youngster appeared to be singularly unconcerned by the circumstances of the interview, and an adequate speech sample was obtained on each occasion.

Subject: 48, Age: 6, Sex: Female

This subject's non-fluency was characterized by rather hypertense, spasmodic blocks on the initial sound of some words. The hypertension was manifested around the lips and in the sudden immobility of the jaw. These blocks were not frequent in occurrence. There appeared to be no significant change in the non-fluent symptoms during the study. The child seemed inclined to withdraw from speaking situations. No interview situation was entirely successful with this child because of the paucity of speech response.

Subject: 49, Age: 7, Sex: Male

This youngster demonstrated a pattern of non-fluency which consisted largely of repetitions. He repeated sounds, syllables, words, and phrases. There were no tonic blocks in evidence. The non-fluency appeared to remain unchanged throughout the course of the investigation. This boy did not hesitate to verbalize during each interview, but he gave the interviewer the impression that he was impatient to complete the interview session as quickly as possible.

Subject: 50, Age: 7, Sex: Male

Analysis of this subject's non-fluency revealed repetitions of syllables and occasional prolongations of sounds in the initial position. The severity and frequency of non-fluency were essentially unaltered during this research. The child seemed willing to participate in the interviews and an adequate sample of speech was obtained during each session.

Subject: 51, Age: 6½, Sex: Male

This child's non-fluency consisted of repetitions of syllables and words. On rare occasions the pattern of speech appeared to be somewhat arhythmic because of the sudden occurrence of pauses between words. The non-fluency did not show improvement during the investigation. The child seemed rather loquacious, and speech utterance was usually obtained without difficulty.

Subject: 52, Age: 6, Sex: Male

This subject demonstrated a non-fluent pattern which included repetitions of syllables, words, and more rarely, phrases. There did not seem to be any evidence of hypertense or spasmodic utterance. There was no significant change in the pattern of non-fluency throughout the course of the study. This child seemed anxious to enter the interview situation. He verbalized quite freely, and cooperation was optimum.

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BIOGRAPHICAL NOTE

Edward M. Penson was born in New York, New York, August 30, 1927. Having majored in Speech with a minor in Psychology, he received his Bachelor of Arts degree, with honors, from the University of Florida, in February 1950. Mr. Penson continued his speech major and psychology minor, and received his Master of Arts degree from Ohio University in February 1951.

In January, 1955, Mr. Penson was appointed Interim Associate to the Speech and Hearing Clinic at the University of Florida. Prior to this appointment, Mr. Penson held the following positions: Clinician; Research Associate in the University of Florida Medical Center Study; and Senior Clinician in the Speech and Hearing Clinic.

Mr. Penson is a Key and Honor member of Sigma Alpha Eta, National Speech and Hearing Honorary Fraternity.

This dissertation was prepared under the direction of the chairman of the candidate's supervisory committee and has been approved by all members of the committee. It was submitted to the Dean of the College of Arts and Sciences and to the Graduate Council and was approved as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

August 13, 1955

C. F. Byers
Dean, College of Arts and Sciences

Dean, Graduate School

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